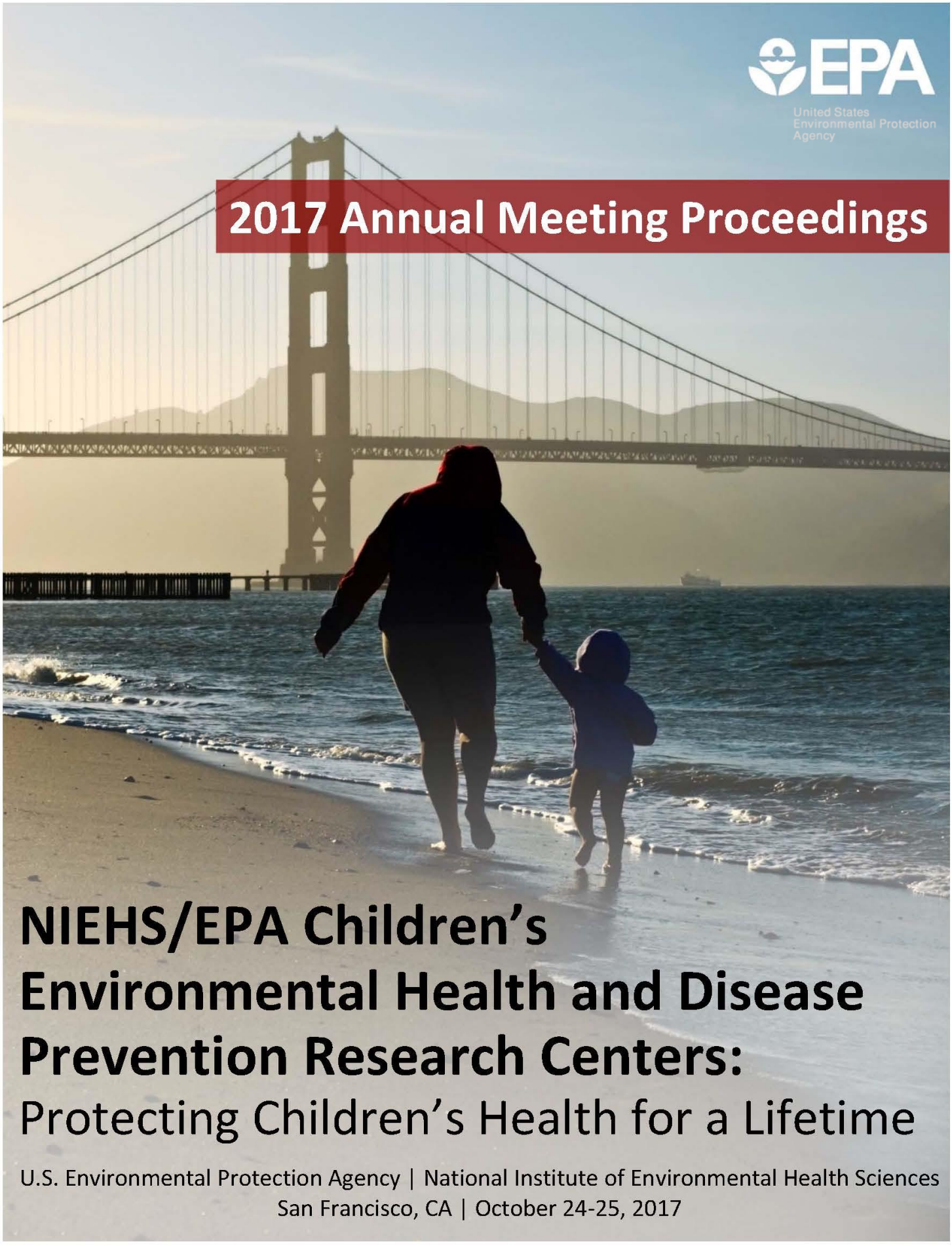

United States Environmental Protection Agency

2017 Annual Meeting Proceedings

NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers:

Protecting Children's Health for a Lifetime

U.S. Environmental Protection Agency | National Institute of Environmental Health Sciences

San Francisco, CA | October 24-25, 2017

National Institute of Environmental Health Sciences
Your Environment. Your Health.

Disclaimer

This document has been reviewed in accordance with U.S. Environmental Protection Agency (EPA) policy and approved for publication. The National Center for Environmental Research, Office of Research and Development was responsible for the preparation of this meeting report. The document provides the abstracts, posters, and presentation slides from the 2017 Annual Meeting of the Children's Environmental Health and Disease Prevention Research Centers (Children's Centers). This program is jointly funded by the EPA under the Science to Achieve Results (STAR) grants program and the National Institute of Environmental Health Sciences. This report is not a complete record of all details discussed. Statements represent the individual views of meeting participants; except as specifically noted, none of the statements represent analyses by or positions of EPA.

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Contents

Proceedings from the 2017 Annual Meeting of the NIEHS/EPA Children's Environmental Health and Disease Prevention Centers Annual Meeting

Day 1 – Tuesday, October 24, 2017

Conference Overview and Welcoming Remarks

- Nica Louie, M.S. | Project Officer, Office of Research and Development (ORD), U.S. Environmental Protection Agency (EPA)
- Kimberly Gray, Ph.D. | Health Science Administrator, National Institutes for Environmental Health Sciences (NIEHS)
- Alexis Strauss, M.A. | Acting Regional Administrator, EPA Region 9
- Claudia Thompson, Ph.D. | Branch Chief, NIEHS
- Elaine Cohen Hubal, Ph.D., M.S. | ORD, EPA

The 2017 Annual Meeting of the NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers was hosted by EPA in collaboration with NIEHS and the Pediatric Environmental Health Specialty Units (PEHSUs). Ms. Nica Louie (EPA) welcomed participants to the meeting held at the EPA Region 9 offices in San Francisco. She thanked EPA Region 9 for accommodating the meeting and Ms. Jacquelyn Menghrajani (EPA Region 9) for her tremendous help during the planning process. Ms. Louie expressed appreciation to the conference steering committee for their efforts in preparing an inclusive and collaborative conference agenda to foster partnership.

Ms. Alexis Strauss, Acting Regional Administrator of EPA Region 9, welcomed the participants to the EPA Region 9 facilities and stated how excited she is that the Children's Centers have convened on the West Coast which has been home to several Children's Centers. Following Ms. Strauss were Dr. Claudia Thompson (NIEHS) and Dr. Elaine Cohen Hubal (EPA), representing leadership from NIEHS and EPA, who discussed how the Children's Centers support the missions of both agencies and the importance of protecting the health of the next generation. Dr. Kimberly Gray (NIEHS) then addressed the participants, setting the stage and expectations for the two-day meeting. Please see Appendix A for a list of the Children's Centers, Appendix B for the meeting agenda, Appendix C for a list of steering committee members, and Appendix D for a list of meeting participants.

Quick Connections

The Quick Connections session provided meeting participants with an opportunity to meet and identify new potential collaborators. Through a series of short conversations, participants were able to share their work and what makes them passionate about children's environmental health. An open networking session replaced the afternoon Quick Connections session to facilitate longer, more in-depth conversations about collaboration.

Progress Review

The meeting then transitioned to the Progress Review sessions, where the centers and PEHSUs were prompted to present posters with the most compelling research finding they have made in the past two years. The progress review poster session was broken into three parts, with five to seven posters being presented simultaneously throughout the conference space during each part. Meeting participants rotated between posters in groups of approximately 15 to 20, listening to short presentations and engaging in small group discussions. Copies of the posters have been provided in Appendix E. Due to concerns about unpublished data, presentations marked with an asterisk have not been included in the appendix.

Progress Review Part I

The first Progress Review session included five poster presentations. Abstracts submitted by the centers for these posters have been provided below. These abstracts and posters reflect the individual views of meeting participants and centers, none of the statements represent analyses by or positions of EPA.

(1) Columbia University | Longitudinal Effects of Prenatal Exposure to Polycyclic Aromatic Hydrocarbons on Mental, Behavioral, and Emotional Disorders as well as Obesity in Adolescence | Frederica Perera, Ph.D., Dr. P.H., Virginia Rauh, Sc.D.
(2) Dartmouth College | Should Rice Cereal be an Infant's First Food? | Carolyn Murray, M.D., M.P.H.
(3) Duke University | Exposure to Tobacco Smoke During Pregnancy – and Even During Preconception – Can Alter Baby's Brain Function | Susan Murphy, Ph.D.
(4) Emory University | African American Women in Metro Atlanta Have Higher Levels of Endocrine Disrupting Plasticizers in Their Bodies Than Other African American Women | P. Barry Ryan, Ph.D., M.S.
(5) Johns Hopkins University | Obesity and Diet as Susceptibility Factors to Air Pollution Exposure | Nadia Hansel, M.D.

(1) Columbia University Center for Children's Environmental Health (CCCEH)

Frederica Perera, Ph.D., Dr. P.H., Columbia University
Virginia Rauh, Sc.D., Columbia University

TITLE: Longitudinal Effects of Prenatal Exposure to Polycyclic Aromatic Hydrocarbons on Mental, Behavioral, and Emotional Disorders as well as Obesity in Adolescence

BACKGROUND: The Columbia University Children's Center is testing the hypothesis that prenatal and early childhood exposures to polycyclic aromatic hydrocarbons (PAHs) disrupt development and maturation of neural systems that support self-regulatory systems in the brain; and these disturbances create vulnerabilities that lead to mental, behavioral, emotional disorders as well as obesity in adolescence.

SPECIFIC AIMS: Specific aims are to test whether: (1) Elevated prenatal PAH exposure is associated with adverse effects on self-regulatory processes, clinical symptoms, and distinctive adverse developmental trajectories from early childhood through ages 15 to 17 years; (2) Maternal exposure to higher concentrations of airborne PAH during pregnancy is associated with distinct growth trajectories of body mass index growth and fat mass index and greater adiposity, higher hedonic eating behavior, sedentary pursuits, and poorer neuropsychological function at ages 15 to 17 years; and (3) Early PAH exposure adversely affects the structure, function, and metabolism of neural systems known to support the capacity for self-regulation at ages 9 to 12 years, and subsequently, these PAH-related disturbances mediate the

emergence of conduct disturbance, substance use, depression, symptoms of attention deficit hyperactivity disorder (ADHD), and adiposity measures through adolescence at ages 15 to 17 years.

KEY RESEARCH FINDINGS: We detected a significant interaction ($p = 0.05$) between PAH-DNA adducts in maternal blood collected at delivery with time, in which the developmental trajectory of self-regulatory capacity was delayed in the exposed children. Multiple linear regression revealed a positive association between the presence of PAH-DNA adducts and problems with social competence ($p < 0.04$), level of dysregulation and problems with social competence ($p < 0.0001$), and evidence that self-regulation mediates the association of prenatal exposure to PAH with social competence ($p < 0.0007$).

PRELIMINARY FINDINGS TO BE EXPANDED: Co-exposure to socioeconomic disadvantage (lack of adequate food, housing, utilities, and clothing) and prenatal PAH significantly increases the risk of ADHD behavior problems, particularly high PAH and persistent hardship. Previously we have reported associations between prenatal exposure to PAH and anatomical changes in children's brains when imaged by magnetic resonance imaging (MRI) at ages 7 to 9 years. Follow-up MRI data at ages 9 to 12 years are currently being analyzed.

CHALLENGES: Initially, researchers experienced delays in participant recruitment and the rate of assessment due to the need to refine the MRI protocol for imaging the brain and abdomen in the same MRI visit, but by scheduling more visits during the summer months and weekends, they are on target to achieve their goals.

(2) Children's Environmental Health and Disease Prevention Research Center at Dartmouth College

Carolyn Murray, M.D., M.P.H., Dartmouth College

TITLE: Should Rice Cereal be an Infant's First Food?

SPECIFIC AIMS: The primary aims of the Dartmouth College Children's Center are to identify environmental exposures to common contaminants such as arsenic during fetal development and childhood; and the impact these exposures have on childhood immunity, growth, and neurological development.

KEY RESEARCH FINDINGS: Maternal dietary exposure through rice consumption results in fetal exposure and may impact risk of later disease risk, in particular, growth, immune-related, gene expression and epigenetic outcomes. In addition to detecting arsenic in rice products, including those targeted to infants, we reported that infants commonly consume these products in the first year of life.

PRELIMINARY FINDINGS TO BE EXPANDED: New results from work of our center's Community Outreach and Translation Core (COTC) indicate that women who receive results of elevated well water arsenic levels report less use of their tap water for drinking, cooking, and for mixing infant formula than women who received reports of low or no arsenic.

CHALLENGES: Effectively communicating our findings about arsenic in food and water to relevant stakeholders presented challenges, particularly as we sought to avoid unintended consequences, such as inappropriate dietary changes. To address this challenge, we held focus groups with study participants, produced web-tools, met with federal agencies and congressional offices, organized an interdisciplinary collaborative, and published scientific reports to reach both the scientific and medical community to inform ways to reduce children's exposure.

(3) Neurodevelopment and Improving Children's Health Following Environmental Tobacco Smoke Exposure (NICHES)

Susan Murphy, Ph.D., Duke University

TITLE: Exposure to Tobacco During Pregnancy – and Even Preconception – Can Alter Offspring's Brain Function

KEY RESEARCH FINDINGS: Exposures to toxic chemicals like those contained in tobacco smoke during early life can lead to permanent changes in the programming of gene activity. The specific window(s) of development during which such programming in the brain is most vulnerable to exposure has not been clearly defined. Female rats were surgically fitted with osmotic mini pumps designed to deliver a defined low-level dose of vehicle-only or tobacco smoke extract during three time intervals before and during gestation, encompassing pre-mating (with termination of exposure prior to mating), early or late gestation. Results showed that the most pronounced reprogramming of neuronal functions was from exposure that occurred during late gestation. Remarkably however, pre-mating exposure also had pronounced effects on neuronal functions. These results show that there is no time interval before or during pregnancy during which tobacco smoke exposure is safe, and that cessation of exposure once pregnancy is established may be too late to prevent detrimental effects. These findings may additionally have substantial implications for the offspring born to women of childbearing age who are exposed to tobacco smoke even prior to conception.

(4) Emory University Center for Children's Health, the Environment, Microbiome, and Metabolomics (C-CHEM2)

P. Barry Ryan, Ph.D., M.S., Emory University

TITLE: American Women in Metro Atlanta Have Higher Levels of Endocrine Disrupting Plasticizers in Their Bodies Than Other African American Women

SPECIFIC AIMS: The Emory University Children's Center is a multi-component investigation designed to evaluate environmental exposures influencing the infant microbiome and leading to neurodevelopmental sequelae in a population of African-American mothers in metropolitan Atlanta.

METHODS: In the first phase, we have collected environmental and biological data on toxicant exposures from samples collected at prenatal and home visits. C-CHEM2's first project, Characterizing Exposures in an Urban Environment (CHERUB), is designed to validate protocols for office and field sampling and determine the relationship between environmental media concentrations and biomarkers relevant to the microbiome of infants. Environmental and biological samples are taken from mothers during pregnancy and in-home environmental samples, prior to delivery. These samples will be analyzed for: bisphenol A (BPA), phthalates, parabens, alkylphenols, organophosphate insecticides, pyrethroid insecticides, air pollutants (PAHs), and brominated flame retardants or appropriate metabolites

KEY RESEARCH FINDINGS: Presently, researchers have collected 212 first hospital visit and 126 second hospital visit urine samples from expectant mothers and followed that with home visits gathering 101 urine samples, 108 serum samples, 101 prenatal home dust samples, 55 postnatal home dust samples, 25 home air samples. In addition, researchers have collected 42 urine samples from babies 1 week old, 28 from babies 3 months old, 14 urine samples from babies 6 months old, and 1 sample from a baby 12 months old. Analysis has been completed for urinary BPA and phthalates, and this data is reported on here. Further, recruitment continues with an ultimate target of 300 participating women and approximately 100 individual homes each monitored several times. Currently researchers have completed approximately one-third of the projected first home visits and started second home visits on early recruits.

CONCLUSIONS: Results for BPA and phthalate metabolites indicate that the study population shows concentrations higher than the national average as measured in NHANES investigations and higher than the African-American sub-population from the same investigations. Analysis continues correlating results from other measures on environmental exposure and biomarkers of such exposure.

(5) Johns Hopkins University Center for the Study of Childhood Asthma in the Urban Environment (CCAUE)

Nadia Hansel, M.D., Johns Hopkins University

TITLE: Obesity and Diet as Susceptibility Factors to Air Pollution Exposure

SPECIFIC AIMS: The Johns Hopkins University Children's Center is currently investigating the role of obesity as a determinant of susceptibly to air pollution among children with asthma. This is a key step in achieving the Center's overall goal of developing strategies to reduce asthma morbidity by modifying indoor allergen and pollutant exposures.

KEY RESEARCH FINDINGS: Recent findings that children who are overweight and obese have increased asthma symptoms in response to secondhand smoke compared to normal weight children builds on the evidence that has been reported by the Center investigators. Obesity is often linked to diet, comorbidities and physical activity thus there are challenges to understanding the different pathways by which obesity may lead to susceptibility. Recent findings of the Center also suggest fatty acid intake may modify susceptibility to indoor air pollution. Furthermore, the high prevalence of obstructive sleep apnea among our children suggests that sleep disordered breathing may be an important consideration as the Center aims to better understand the complex interactions between obesity and pollution susceptibility. The Center's work with low-income children with asthma in Baltimore City reveals the environmental challenges faced by families in real-world settings that must be overcome to improve health disparities.

Progress Review Part II

The second Progress Review session included six poster presentations. Abstracts submitted by the centers for these posters have been provided below. These abstracts and posters reflect the individual views of meeting participants and centers, none of the statements represent analyses by or positions of EPA.

(6) Northeastern University | Exposure to Triclosan in Pregnancy is Associated with Increased Inflammation | Akram Alshawabkeh, Ph.D., John Meeker, Sc.D.

(7) University of California, Berkeley (CERCH) * | Mixtures of Pesticides Used near Homes During Pregnancy Associated with Decreased IQ in Children | Kim Harley, Ph.D.

(8) University of California, Berkeley (CIRCLE) | Toxic PCBs Still Harming Children, Despite Long-Time Ban | Todd Whitehead, Ph.D.

(9) University of California, Berkeley/Stanford University | Ambient Air Pollution Impairs Immune Function, which Impacts Allergy and Asthma | S. Katharine Hammond, Ph.D.

(10) University of California, Davis | Neonatal Cytokine Profiles Associated with Autism Spectrum Disorder| Judy Van de Water, Ph.D.

(11) PEHSU Region 2* | Effectively Integrate Environmental Health into Clinical Practice | Perry Sheffield, M.D.

(6) Northeastern University Center for Research on Early Childhood Exposure and Development in Puerto Rico (CRECE)

Akram Alshawabkeh, Ph.D., Northeastern University
John Meeker, Sc.D., University of Michigan

TITLE: Exposure to Triclosan in Pregnancy is Associated with Increased Inflammation

SPECIFIC AIMS: The Northeastern University Children's Center studies the impact of a mixture of environmental exposures and modifying factors on fetal and early childhood health and development in the children of the heavily-contaminated northern coast of Puerto Rico – an underserved, highly-exposed, and low-income population with significant health disparities. CRECE has developed an innovative and scientifically distinct program that leverages the ongoing cohort study of the PROTECT NIEHS Superfund Research Center. CRECE is following-up 600 infants born to the PROTECT cohort, for whom a rich prenatal dataset and biological samples already exist, following them from birth to age four. CRECE is (1) capturing the impacts of pollutant exposures that occur through multiple exposure routes and biological pathways on fetal and early childhood health and development, (2) evaluating how psychosocial risk factors (e.g. socioeconomic status and maternal stress) may modify these effects, and (3) elucidating biological mechanisms that may explain mechanistic pathways and mediate these relationships.

KEY RESEARCH FINDINGS: Urinary concentrations of triclosan (TCS) in urine samples collected from the study participants were higher than among women of reproductive age in the US general population, with positive associations between TCS concentrations with self-reported use of liquid soap. Further, findings suggest that exposure to TCS during pregnancy may be related to inflammation, which may influence birth outcomes and other adverse health effects. These TCS findings are timely for aiding in preventive public health policy and practice. In September 2017, the U.S. Food and Drug Administration announced it was prohibiting chemicals, including triclosan, triclocarban, and 17 other chemical ingredients, in products such as hand soaps and toothpaste.

PRELIMINARY FINDINGS TO BE EXPANDED: In the Center's preliminary data, the PIs have reported evidence for increased exposures to several phenols compared to women of reproductive age from the NHANES study. We have also investigated preliminary associations between maternal urinary concentrations of phenols/parabens and biomarkers of intermediate effect during pregnancy, and found a significant positive association between TCS and IL-6 (a pro-inflammatory cytokine), significant associations between numerous phenols/parabens and increased levels of the oxidative stress marker 8-isoprostane, and several associations between phenols or parabens and altered reproductive or thyroid hormone levels. CRECE is also examining the association between air pollutant exposures and development in a cohort of young children living in Puerto Rico, whom they will follow from gestation through age four. CRECE does so using traditional measures of adverse birth outcomes and development, such as preterm birth and respiratory and neurodevelopmental evaluations, and using novel measurements of non-nutritive suck, an established measure of newborn central nervous system function that has not yet been used to assess neonatal development in environmental epidemiological studies. By linking these health measures to air pollution exposures, in utero chemical exposures, and maternal and child characteristics for each child, the Center will examine whether ambient pollution exposure alters the developing brain, a susceptible organ that is difficult to access in a clinical evaluation.

CHALLENGES: The implications of Hurricane Maria and staff supporting recovery efforts.

(7) University of California, Berkeley Center for Environmental Research and Children's Health (CERCH) *

Kim Harley, Ph.D., University of California, Berkeley

HEADLINETITLE: Mixtures of Pesticides Used near Homes During Pregnancy Associated with Decreased IQ in Children

SPECIFIC AIMS:

1) To determine whether prenatal exposure to organophosphate pesticides (OPs) and pesticide mixtures is associated with:
   a) Behavior (externalizing and risk-taking behaviors, school failure, delinquency) at age 18 years;
   b) Brain function (NIH toolbox, functional near infrared spectroscopy (fNIRS)) at age 18 years;
   c) Body mass index (BMI) and metabolic conditions (hypertension, diabetes, fatty liver) at ages 18 and 21 years;
   d) Respiratory illness and lung function at ages 18 and 21 years;

2)To determine whether these associations are modified by poorer cognition/attention, or by early life adversities or protective factors.

3)To determine the contribution of early adversity on the emergence of risk-taking behavior and early puberty.

4)To determine the relationship between paraben and phenol exposure on obesity and metabolic syndrome, biomarkers of oxidative stress, puberty timing, thyroid function, and lung function.

5)To determine the relationship between phthalate exposure and neurodevelopment, obesity and metabolic syndrome, biomarkers of oxidative stress, puberty timing, thyroid function, lung function, and epigenetic changes in blood.

KEY RESEARCH FINDINGS: CERCH has used California's Pesticide Use Reporting (PUR) system to confirm the associations of in utero organophosphate pesticide exposure with child neurodevelopment that was observed using urinary dialkyl phosphate (DAP) metabolites, this time using residential proximity to agricultural pesticide use. This methodology allows researchers to examine other neurotoxic pesticides besides OPs and also to examine mixtures of many pesticides that are used simultaneously in agriculture. They observed a decrease of 2.2 points [95% confidence interval (CI): −3.9, −0.5] in Full-Scale IQ and 2.9 points (95% CI: −4.4, −1.3) in Verbal Comprehension for each standard deviation increase in toxicity-weighted use of organophosphate pesticides, and similar decrements in Full-Scale IQ at 7-years of age with each standard deviation increase of prenatal use of two organophosphates and three other neurotoxic pesticide groups. Using Bayesian profile regression, CERCH researchers examined associations between clustered neurotoxic pesticide use profiles and childhood Full-Scale IQ. Two of the eight distinct pesticide profile clusters exhibited some of the highest cumulative neurotoxic pesticide use levels and were associated with deficits in adjusted Full-Scale IQ of -6.9 (95% credible interval: -11.3, -2.2) and -6.4 (95% credible interval: -13.1, 0.49), respectively, when compared with the pesticide profile cluster that showed the lowest level of pesticides use. CERCH also found that residential proximity to OP and carbamate pesticide use during pregnancy and both household- and neighborhood-level poverty during childhood were independently associated with poorer cognitive functioning in children at 10 years of age and that the previously observed adverse associations between DAP concentrations and IQ were stronger in children experiencing greater early childhood adversity.

PRELIMINARY FINDINGS TO BE EXPANDED: Prenatal urinary concentrations of chemicals used in personal care products (specifically monoethyl phthalate (MEP) and triclosan) are associated with earlier puberty in girls. CERCH researchers found that each doubling of maternal urinary concentrations of triclosan during pregnancy was associated with a 0.6 month earlier shift in age at menarche. Each doubling of MEP metabolites in maternal urine during pregnancy was associated with a 1.2 month earlier shift in pubic hair

development. Models controlled for family income, mother's education, mother's years of residence in US, and mother's diet quality index in pregnancy.

(8) University of California, Berkeley Center for Integrative Research on Childhood Leukemia and the Environment (CIRCLE)

Todd Whitehead, Ph.D., University of California, Berkeley

TITLE: Toxic PCBs Still Harming Children

BACKGROUND: The University of California, Berkeley CIRCLE Children's Center been invested in measuring children's exposure to polychlorinated biphenyls (PCBs) and assessing the impact of these exposures.

KEY RESEARCH FINDINGS: Despite being banned for several decades, PCBs are still readily detected in the settled dust of California homes and in the blood of children who live there. Furthermore, CIRCLE researchers have observed associations between the levels of PCBs in the dust of a child's home and his/her risk of childhood leukemia.

PRELIMINARY FINDINGS TO BE EXPANDED: In the current cycle, the Center is working to identify the mechanisms responsible for the observed association between PCB exposure and increased leukemia risk. Researchers are investigating the relationship between PCB contamination and levels of the immunomodulatory cytokine, IL-10, at birth - as a marker of abnormal fetal immune development. CIRCLE researchers are also looking at how PCB contamination in homes might be related to changes in DNA methylation. Finally, CIRCLE is using a mouse model of childhood leukemia to observe changes in cytokine levels and DNA methylation after controlled exposure to a mixture of PCBs in utero, to further elucidate the potential biological mechanisms at play.

(9) University of California, Berkeley/Stanford University Children's Environmental Health Center (CHAPS)

S. Katharine Hammond, Ph.D., University of California, Berkeley

TITLE: Ambient Air Pollution Impairs Immune Function, which Impacts Allergy and Asthma

KEY RESEARCH FINDINGS: In earlier work, CHAPS researchers showed that exposure to ambient air pollution was associated with hypermethylation of the forkhead box protein 3 (FOXP3) locus, impairing regulatory T-cell (Treg) function and increasing risk of asthma morbidity. In a later follow-up study with a larger sample size, CHAPS researchers showed that exposure to ambient PAHs in Fresno, CA was significantly associated with impaired Treg function, increased methylation of FOXP3, and differential expression of the FOXP3 protein, especially in children with allergies. Methylation was associated with Treg dysfunction and an increase in total plasma immunoglobulin E (IgE) levels. These findings were supported by those of another group that reported FOXP3 hypermethylation was associated with diesel exhaust exposure and risk for childhood asthma. CHAPS researchers have also shown that ambient PAH exposure is associated with increased respiratory symptoms in children with asthma as well as lower lung function in children without asthma in Fresno. In addition to exposure to PAHs, CHAPS researchers have recently shown that short-term and long-term exposures to high levels of carbon monoxide (CO), nitrogen dioxide (NO_2), and fine particulate matter ($PM_{2.5}$) were associated with alterations in CpG site methylation of FOXP3 and interleukin 10 (IL-10). Collectively, these results demonstrate that increased exposure to traffic-related air pollution is associated with impaired systemic immunity and epigenetic modifications in a key locus involved in allergy: FOXP3, with a higher impact on allergic children. The results suggest that increased exposure to air pollution are linked to increased allergic and asthmatic symptoms in children.

(10) University of California, Davis Center for Children's Environmental Health and Disease Prevention

Judy Van de Water, Ph.D., University of California, Davis

TITLE: Neonatal Cytokine Profiles Associated with Autism Spectrum Disorder

SPECIFIC AIMS:

- Leverage the vast research resources generated by the retrospective case-control study, Childhood Autism Risk from Genes and Environment (CHARGE Study) and the prospective cohort study, Markers of Autism Risk in Babies--Learning Early Signs (MARBLES Study).
- Build upon our novel findings of calcium dysregulation in cultured neurons and immune cells in the context of understanding the epigenetic effects and ramifications of toxicant exposure on gene pathways and immune function.
- Develop and apply new biomarkers of autism risk, through analysis of gestational and neonatal immune dysfunction, genetic susceptibility, and environmental exposures, to best characterize the potential health effects at various life stages and predict longer-term clinical and behavioral consequences.

CHALLENGES: A challenge was to produce human iPSC-derived neurons with mature phenotypes in a consistent and robust manner. The Center's response was to develop alternative human cell-based modes: (1) LUHMES neuronal cell line; (2) differentiation of human epidermal neural crest cells into neurons.

(11) PEHSU Region 2*

Perry Sheffield, M.D., Icahn School of Medicine at Mount Sinai

The Mount Sinai P30 Community Engagement Core (CEC) along with the Region 2 PEHSU has partnered with the University of Cincinnati P30 CEC and Region 5 PEHSU at Cincinnati Children's Hospital to more effectively integrate environmental health into clinical practice, using a P30 supplement from NIEHS. This project incorporates environmental health education into electronic health records and web platforms which will allow clinicians to: (1) educate, counsel and refer families using evidence-based outreach and education from local, state and federal agencies including NIEHS CECs as well as the PEHSU national network, and (2) connect families to needed environmental health services to prevent and reduce common environmental exposures in the home. Our diverse expert panel includes 4 CECs and 4 PEHSUs across federal Regions 1,2,3 and 5 (Harvard/Boston Children's, University of Rochester, WEACT, University of Pennsylvania, Georgetown School of Nursing).

Progress Review Part III

The third Progress Review session included six poster presentations. Abstracts submitted by the centers for these posters have been provided below. These abstracts and posters reflect the individual views of meeting participants and centers, none of the statements represent analyses by or positions of EPA.

(12) University of California, San Francisco | Flame Retardants Linked to Lower Child IQ | Tracey Woodruff, Ph.D., M.P.H.

(13) University of Illinois* | Through the Window of a Baby's Eyes | Susan Schantz, Ph.D.

(14) University of Michigan* | A Tale of Environmental Deflection in Mice and Humans: Toxicant Exposures and Lifestyle Factors Influence the Rate of Epigenetic Aging | Jaclyn Goodrich, Ph.D.

(15) University of Southern California | Does Air Pollution Cause Childhood Obesity and Increase the Risk of Diabetes? | Rob Scot McConnell, M.D.

(16) University of Washington | Longitudinal Exposome Research Reveals Exposure of Agricultural Families to Over 86 Pesticides, 47 of Which May Impact Neurodevelopment in Young Children | Elaine Faustman, Ph.D.

(17) PEHSU Region 9 | A Story of Health Multimedia eBook Improves Environmental Health Literacy of Thousands of Health Professionals | Mark Miller, M.D.

(12) University of California, San Francisco Pregnancy Exposures to Environmental Chemicals (PEEC) Children's Center

Tracey Woodruff, Ph.D., M.P.H., University of California, San Francisco

TITLE: Flame Retardants Linked to Lower Child IQ

BACKGROUND: The University of California, San Francisco Children's Center evaluates chemical exposures during pregnancy and the links to development, whether health effects are enhanced by exposure to chronic psychosocial stress, and the role of the placenta as an etiologic pathway. The PEEC Center uses their findings along with those from other Children's Centers to inform the public, clinicians, and policy decision makers about the science and best approaches to reduce harmful chemical exposures across the population.

KEY RESEARCH FINDINGS: One of the Center's recent research findings uses systematic review methods, developed by this program, to conclude that there is sufficient evidence supporting an association between prenatal exposure to polybrominated diphenyl ether (PBDE) flame retardants and lower child IQ. A recent report by the National Academies of Sciences endorsed the study and integrated evidence from animal studies to reach similar conclusions that PBDEs are a "presumed hazard" to intelligence in humans. As part of the center's aims, researchers will continue to explore and publish data, information, and resources about exposures in our population, including PDBEs and other chemical exposure, and what that means for our reproductive health and future.

(13) University of Illinois Novel Methods to Assess the Effects of Chemicals on Child Development*

Susan Schantz, Ph.D., University of Illinois

TITLE: Through the Window of a Baby's Eyes

KEY RESEARCH FINDINGS: The Illinois Children's Center uses a unique approach to assess cognitive function very early in development. The center is studying the impact of various maternal factors on infant cognition. These include maternal obesity and prenatal stress, as well as prenatal exposures to a variety of endocrine disrupting chemicals. Our approach uses infrared eye tracking to record the looking behavior of infants as they study stimuli and videos displayed on a large-screen high-definition TV. Recent findings suggest that maternal prenatal stress adversely impacts physical reasoning in 4-month old female infants, and that higher prenatal bisphenol F (BPF) exposure is associated with poorer visual recognition memory in 7-month old infants.

(14) University of Michigan Lifecourse Exposures and Diet: Epigenetics, Maturation, and Metabolic Syndrome*

Jaclyn Goodrich, Ph.D., University of Michigan

TITLE: A Tale of Environmental Deflection in Mice and Humans: Toxicant Exposures and Lifestyle Factors Influence the Rate of Epigenetic Aging

BACKGROUND: The overall goals of the University of Michigan Children's Center are to determine whether in utero and peri-pubertal exposures to endocrine disrupting chemicals (EDCs) affect physical growth, tempo of sexual maturation, and metabolic homeostasis, and to examine biological mechanisms underlying these effects in rodent and human models. Epigenetics is one of the mechanisms studied throughout the center in the agouti mouse model, the Michigan Mother-Infant Pairs (MMIP) cohort, and the Early Life Exposures in Mexico to Environmental Toxicants (ELEMENT) cohort. The epigenome is an alterable regulatory framework that governs the response of cells and tissues to environmental stressors. DNA methylation is one class of epigenetic modifications that is relatively stable at many loci but known to change across the lifespan at others. While accelerated epigenetic aging at these loci is associated with overall mortality, obesity, cancer, and more, few studies have identified specific environmental factors that influence the rate of change.

SPECIFIC AIMS: 1) Identify loci where DNA methylation changes over time in surrogate tissues from mice and humans. 2) Determine whether EDC exposures and diet early in life modify the rate of epigenetic change.

KEY RESEARCH FINDINGS: Recently, investigators published a contemporary review in Toxicological Sciences introducing the concept of environmental deflection which encompasses toxicant- and nutrient-mediated shifts away from the baseline rate of epigenetic aging. In the agouti mouse model, center investigators first examined the influence of perinatal Western high fat diet or Mediterranean high fat diet with or without concurrent BPA exposure on age-related DNA methylation change in matched tail and blood DNA samples from 2, 4, and 10 months of age. Results, published in Reproductive Toxicology, support environmental deflection as perinatal exposure to a Western diet modified the rate of change in murine tail DNA methylation over time at IAP repetitive elements and Esr1.

PRELIMINARY FINDINGS TO BE EXPANDED: In the ELEMENT birth cohort, the Center is currently investigating environmental deflection by lead, phthalates, and BPA in matched blood DNA samples from birth, early adolescence, and late adolescence at genes related to growth and metabolic outcomes as well as throughout the epigenome using the Infinium MethylationEPIC platform. DNA methylation analysis was also performed in cord blood samples from the MMIP cohort along with first trimester exposure assessment. Plans to follow-up MMIP children, funded by the NIH Environmental influences on Child Health Outcomes (ECHO) program, will provide an opportunity to examine environmental deflection by prenatal EDC exposures among these young children. Overall, the University of Michigan Center is at the forefront of identifying early life environmental and lifestyle factors that deflect rates of epigenetic aging which may ultimately contribute to adverse health outcomes in childhood, adolescence, and adulthood.

(15) University of Southern California Children's Environmental Health Center

Rob Scot McConnell, M.D., University of Southern California

TITLE: Does Air Pollution Cause Childhood Obesity and Increase the Risk of Diabetes?

BACKGROUND: The epidemic of childhood obesity threatens the health of a generation of children because it is a major risk factor for type 2 diabetes, non-alcoholic fatty liver disease and cardiovascular diseases (CVD).

SPECIFIC AIMS: The University of Southern California Children's Center's integrated program of population-based, clinical and experimental research addresses the hypothesis that air pollution contributes to development of childhood obesity and metabolic and inflammatory abnormalities that increase the risk of type 2 diabetes and cardiovascular disease.

KEY RESEARCH FINDINGS: Investigators have found that near-roadway air pollution, in synergy with secondhand tobacco smoke exposure, was associated with a trajectory of increasing BMI over the course of adolescence. Previous year exposure to ambient $PM_{2.5}$ was associated in cross-sectional analyses with 25 percent higher fasting insulin, 8.3 percent lower insulin sensitivity, 14.7 percent higher acute insulin response to glucose and 1.7 percent higher fasting glucose (all $p < 0.001$) in minority children. Associations of increased NO_2 and near-roadway air pollution exposure were also observed with these outcomes. Higher levels of NO_2 and $PM_{2.5}$ were associated with a faster decline in longitudinally collected measures of insulin sensitivity (SI) and obesity in overweight and obese Latino children, and with a lower SI at age 18 years. Increased NO_2 exposure was associated with faster decline in disposition index (DI) and a lower DI at age 18, indicative of adverse effects on B-cell function. Higher levels of NO_2 and traffic exposure were associated with increased levels of cytokeratin-18, a marker for hepatic apoptosis. Mice exposed prenatally to PM had subsequent increased weight gain and fat mass, increased anxiety-like behavior, disrupted circadian activity patterns, and impaired glucose tolerance in a sexually dimorphic pattern. Thus, elevated air pollution exposure may cause a metabolic profile characteristic of increased risk for type 2 diabetes. Innovative infographic and online tools have been developed for communicating risks and uncertainties to communities and to housing and parks planners and policy makers faced with balancing the need for these services and reducing residential near-roadway air pollution exposure.

(16) University of Washington Center for Child Environmental Health Risks Research

Elaine Faustman, Ph.D., University of Washington

TITLE: Longitudinal Exposome Research Reveals Exposure of Agricultural Families to Over 86 Pesticides, 47 of Which are Identified as Developmental Neurotoxicants

SPECIFIC AIMS:

- Identify cellular, biochemical and molecular mechanisms for the adverse developmental neurotoxicity of pesticides;
- Identify susceptibility factors for developmental neurotoxicity of pesticides;
- Improve our understanding of risks from children's exposure to pesticides; and to
- Develop interventions to reduce children's exposure to pesticides.

KEY RESEARCH FINDINGS: The theme of the University of Washington Children's Center has been to understand the mechanisms (molecular, genetic, age, exposure and social factors) that define children's susceptibility to pesticides, identifying the implications of this susceptibility for development and learning, and partnering with communities to translate findings into risk communication, risk management and prevention strategies. This poster shows critical pathways of pesticide exposure for children in farmworker and non-farm worker families and shows how interventions are shown to reduce children's exposure to pesticides. The center is organized using a Risk Assessment Framework that facilitates the incorporation and use of state-of-the-art science to inform risk decisions. A critical premise for the center is its commitment to Community Based Participatory Research and this commitment allowed investigators to overcome and investigate the complex patterns of exposure for short-lived and episodic pesticide use that agricultural communities can experience.

(17) PEHSU Region 9/University of California, Berkeley CIRCLE

Mark Miller, M.D., PEHSU Region 9

TITLE: “A Story of Health” Multimedia eBook Improves Environmental Health Literacy of Thousands of Health Professionals

KEY RESEARCH FINDINGS: Narrative approaches are emerging as powerful health promotion tools that can increase understanding of the determinants of health and translate complex science. “A Story of Health” multimedia eBook and continuing education course were designed to harness the power of storytelling to improve environmental health literacy for health professionals and others. The peer-reviewed eBook uses fictional stories to convey how multiple environmental factors affect health across the lifespan, encourage inclusion of anticipatory guidance, and stimulate policy changes. Readers can explore risk factors for asthma, developmental disabilities and childhood leukemia. A new chapter on reproductive health/infertility has just been released. Each story features the latest research about disease origin and prevention and examines how our natural, built, chemical, food and socioeconomic environments interact with our genes to influence health. Content was drawn from the collective expertise of the PEHSU network and the NIEHS/EPA Children’s Centers, among others. Each story is enriched with illustrations, videos, and links to hundreds of online resources and references. Free continuing education courses are offered through the Centers for Disease Control (CDC) Agency for Toxic Substances and Disease Registry (ATSDR). The eBook provides an alternative method of developing competency in environmental health, as it can be accessed online and reviewed at an individual’s time and pace. Over 8,000 health professionals have registered for the course and evaluations have been overwhelmingly positive. The “Story of Health” eBook is available online.

Day 2 – Wednesday, October 25, 2017

Lightning Talks

The second day of the meeting began with a series of five-minute presentations geared toward sharing successful communication tools and approaches to improve children's environmental health that may be adaptable for different communities. These presentations were categorized into tools targeted to different populations, including pregnant women, parents, children, adolescents, and medical and child care professionals. Following the short presentations, participants broke into small groups to discuss the tools presented and how they may be adapted for different communities. Abstracts for the lightning talks have been included below. These abstracts and posters reflect the individual views of meeting participants and centers, none of the statements represent analyses by or positions of EPA.

Tools Targeted to Pregnant Women and Parents

Moderator: Carmen Marsit, Ph.D., Emory University

(1) Know Better, Live Better: The Development and Implementation of an Environmental Health Social Impact Campaign for African American Women | Abby Mutic, M.S.N., Emory University
(2) Communication Tools for Parents and Caregivers | Kimberly Burke, M.P.H., Columbia University
(3) Disseminating Pesticide Exposure Results to Farmworker and Nonfarmworker Families in Agricultural Community, A Community-Based Participatory Research Approach | Elaine Faustman, Ph.D., University of Washington
(4) Toxic Matters | Annemarie Charlesworth, M.A., University of California, San Francisco
(5) NIEHS/EPA Children's Centers Impact Report | Nica Louie, M.S., EPA; Hayley Aja, M.P.H., EPA Student Contractor; Emily Szwiec, M.P.H., Association of Schools and Programs of Public Health (ASPPH)/EPA

(1) Know Better, Live Better: The Development and Implementation of an Environmental Health Social Impact Campaign for African American Women

Abby Mutic, M.S.N., Emory University

The Emory University Children's Center is investigating the influence of environmental exposures on perinatal outcomes of African American women and children in metro Atlanta. In partnership with the Stakeholder Advisory Board, the center has developed educational materials for dissemination through a broader social media campaign, which involved a short documentary introducing the concept of environmental exposures in a culturally relevant way. As part of the social media campaign, the center is implementing Hootsuite and Facebook analytic tools to capture quantitative data on the impact of the messaging campaign within the target audience. This will allow the center to determine which items attracted the most attention, by whom, and will result in an increased understanding of viewers. This data will also be used to inform the future direction of the Emory University Children's Center social media campaign.

(2) Communication Tools for Parents and Caregivers

Kimberly Burke, M.P.H., Columbia University

The Columbia University Children's Center uses a tiered approach to environmental health communication with parents through a combination of workshops, tip sheets and promotion of mobile application tools. The center's research on common urban pollutants are highlighted during workshops. Tip sheets from the center's "Healthy Home, Healthy Child" campaign are also used to reinforce holistic methods for reducing exposures to harmful chemicals. The mobile applications are tested in a focus group with parents from the center's cohort and focus on green cleaning, green tips, shopping guides for food and for personal care products, as well as climate resiliency/extreme heat.

(3) Disseminating Pesticide Exposure Results to Farmworker and Nonfarmworker Families in an Agricultural Community, A Community-Based Participatory Research Approach

Elaine Faustman, Ph.D., University of Washington

While the University of Washington Children's Center has been committed to returning individual results of pesticide exposure to study participants, there have been challenges in developing individual risk messages from complex scientific data. The center worked with the community on new tools for interpreting exposure and susceptibility. Two town forums were held to identify the best ways to share the pesticide exposure data, and three types of graphical information for individual data were tested. The most popular approach was a thermometer that graphically presents the data using a combination of color gradients and relative values. On follow-up, over 70 percent of participants recalled the graphic and correctly interpreted the results.

(4) Toxic Matters

Annemarie Charlesworth, M.A., University of California, San Francisco

The University of California, San Francisco Children's Center developed "Toxic Matters" to begin conversations between clinicians and their patients focused on preventing exposures at home, work, and in the community, as well as how to become a smart consumer and knowledgeable in environmental health issues. Additionally, the center worked to embed environmental health in medical education including in medical textbooks, lectures, electives, and the Life Stages curriculum. The center also produced a series of short videos, "60 MiNueTs" (available online), that explore the growing impact of environmental chemicals on children's health - including increasing rates of asthma, ADHD, autism, and childhood cancer – and interviews with renown medical experts and scientists.

(5) NIEHS/EPA Children's Centers Impact Report

Nica Louie, M.S., EPA
Hayley Aja, M.P.H., EPA Student Contractor
Emily Szwiec, M.P.H., ASPPH

In October 2017, EPA and NIEHS successfully launched the Children's Centers Impact Report, which is now available online. The landmark report presents select publications that highlight some of the important contributions the centers have made toward reducing the burden of environmentally induced or exacerbated diseases placed on children. The report provides examples of success in the community in support of public health. It is organized in three sections: health outcomes, environmental exposures, and hallmark features. The health outcomes section presents scientific findings from the Children's Centers on several diseases that affect children. The environmental exposures section presents research findings on chemicals and pollutants children are commonly exposed to through air, water, and food. The hallmark features section highlights the unique features

that have facilitated the work of the Children's Centers and advancements in the field. The presentation included an overview on how the report was developed and a guide for how to navigate the document. Discussions that followed the presentation focused on ideas for dissemination of the report.

Tools Targeted to Children and Adolescents

Moderator: Susan Murphy, Ph.D., Duke University

(6) Improving Environmental Health Literacy of Adolescents and Young Adults: Research to Real Life | Mark Miller, M.D., M.P.H., PEHSU Region 9, University of California, Berkeley CIRCLE
(7) Break the Cycle of Children's Environmental Health Disparities in Poor Communities | Leslie Rubin, M.D., PEHSU Region 4
(8) Youth Participatory Action Research: Strengthening Community Communication | James Nolan, M.P.H., University of California, Berkeley CERCH
(9) Empowering Children through Environmental Health Literacy: Moving beyond didactic guest lectures | Nathan Mutic, M.S., M.A.T., M.Ed., Emory University

(6) Improving Environmental Health Literacy of Adolescents and Young Adults: Research to Real Life

Mark Miller, M.D., M.P.H., PEHSU Region 9, University of California, Berkeley CIRCLE

The University of California, Berkeley CIRCLE COTC collaborated with the Region 9 PEHSU on a project titled "Improving Environmental Health Literacy of Young Adults". The intent was to create awareness of the role of pre-conception and prenatal environmental influences on the development of childhood leukemia and other diseases including developmental disabilities, asthma, and reproductive health. The video, "Love in the Time of Toxicants" encourages young adults and prospective parents to learn more about safe products and practices to reduce environmental exposures and enhance lifelong health for themselves and for their children. Additional outreach materials include illustrated books, bookmarks, and informational handouts. These outreach materials are available online.

(7) Break the Cycle of Children's Environmental Health Disparities in Poor Communities

Leslie Rubin, M.D., PEHSU Region 4

Region 4 PEHSU, in collaboration with community and academic partners, has established a program called "Break the Cycle of Children's Environmental Health Disparities". This is a collaborative, interdisciplinary research and training program that encourages and inspires university students to develop creative projects that will reduce or prevent environmental health related illnesses and disorders of children who live in poor communities. "Break the Cycle" offers a readily replicable and reasonably inexpensive model for exploring children's environmental health disparities within the community context, and in cultivating future leaders who will continue to make a positive difference for the health of children, their families and their communities.

(8) Youth Participatory Action Research: Strengthening Community Communication

James Nolan, M.P.H., University of California, Berkeley CERCH

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) Youth Council engages CHAMACOS study participants and other high school aged youth in Salinas Valley, California. The CHAMACOS Youth Council addresses environmental health challenges in the community and works with CERCH researchers to identify environmental health issues, design and conduct research projects, and disseminate study results and education materials in their community. In the CHAMACOS of Salinas Evaluating Chemicals in Homes & Agriculture (COSECHA) study, youth measured pesticide exposures to adolescent girls in the Salinas Valley using personal monitoring wristbands, dust samples, and GPS monitoring. The Salinas youth have taken the lead on developing education and outreach activities. Specific examples include: a radio series for farmworkers on how to reduce potential pesticide exposures; a bilingual video teaching community members how to learn what pesticides have been used in the fields near their homes; a bilingual presentation for children of farmworkers; highlights of their work for local news; and presentations to key stakeholders.

(9) Empowering Children through Environmental Health Literacy: Moving Beyond Didactic Guest Lectures

Nathan Mutic, M.S., M.A.T., M.Ed., Emory University

Public school systems are an accessible platform for disseminating children's environmental health education, and the Children's Centers and PEHSUs are uniquely poised to share current research findings with the children most impacted by their environment. In most modern, digitally-enriched learning environments, there are a myriad of ways Children's Centers and PEHSUs can enhance the classroom experience beyond the traditional didactic guest lecturer approach. As many districts are moving toward non-traditional approaches to curriculum and instruction such as career pathway models and asynchronous online education, partnerships with universities and other community stakeholders are becoming increasingly more common as school administrators seek novel and relevant experiences for their students.

Tools Targeted to Professionals

Moderator: Susan Buchanan, M.D., PEHSU Region 5

(10) **Which Environment? Shifting Communication Strategies to Meet Child Care Provider Needs** | Brenda Davis Koester, M.S., University of Illinois

(11) **Environmental Health Education for Health Professionals** | Carmen Milagros Velez Vega, Ph.D., M.S.W., University of Puerto Rico

(12) **Environmental Health Screening Tools to be Used by Head Start Teachers** | Robin Lee, M.P.H., R.D.N., University of Michigan

(13) **Children's Environmental Health Basics for Early Intervention and Infant Development Professionals** | Jacqueline Barkoski, Ph.D., M.P.H., University of California, Davis

(10) Which Environment? Shifting Communication Strategies to Meet Child Care Provider Needs

Brenda Davis Koester, M.S., University of Illinois

It is especially important to focus on child care providers in environmental health education campaigns, as a majority of children under the age of five are in out-of-home care. In conjunction with the Community Advisory Board, the center initially developed a public service announcement (PSA) animated video addressing endocrine disrupting chemicals and children's health. While the video was very well-received by the child care community, researchers learned through working with the community that the base knowledge about environmental influences on children's health is very low, and that the child care community is eager to learn more practical ways they can implement changes in their day care centers and homes. The center restructured the messaging campaign to provide more basic overviews of what constitutes children's environmental health and examples of good practices rather than focus solely on endocrine disruptors, and are now implementing a variety of messaging tools such as Buzzfeed, Facebook, Twitter, and Pinterest to complement the PSA video.

(11) Environmental Health Education for Health Professionals

Carmen Milagros Velez Vega, Ph.D., M.S.W., University of Puerto Rico

While health clinic professionals in Puerto Rico are somewhat aware of the specific contaminants and health effects studied by the Northeastern University Children's Center, they are largely unaware of the broader relationship between environment and disease. In order to quantify this observation, center clinic staff conducted surveys to gauge environmental health knowledge of health providers in Puerto Rico. In order to fill this knowledge gap, center researchers and COTC staff give formal presentations at clinics and hospitals on current research, teach clinic staff to use research equipment, present to numerous audiences on Zika prevention, and educate masters students on environmental health.

(12) Environmental Health Screening Tools to be Used by Head Start Teachers

Robin Lee, M.P.H., R.D.N., University of Michigan

The University of Michigan Children's Center's COTC has worked closely with their Community Advisory Board in Kent County, MI, to develop environmental health screening tools to be used by Head Start teachers during home visits and during parent meetings. One tool is a survey that would be administered to parents at Head Start Parent Coalition Meetings to understand their level of concern and knowledge on environmental hazards their children may face in the home setting. From this survey, researchers can then tailor the resources and information provided to Head Start teachers to educate parents on environmental hazards in the home. The other tool is an adapted visual checklist for Head Start teachers to assess environmental health hazards to students during annual home visits. Teachers can then refer families in high-risk homes to the appropriate resources, including partner Healthy Homes Coalition of West Michigan. This visual screening tool is meant to be a quick and simple method for Head Start teachers to evaluate the environmental health of their students' homes. The center hopes to pilot these tools with Head Start for Kent County during the 2018-2019 school year, evaluate the processes and effectiveness of these tools, and adapt the tools to meet the community's needs.

(13) Children's Environmental Health Basics for Early Intervention and Infant Development Professionals

Jacqueline Barkoski, Ph.D., M.P.H., University of California, Davis

The "Children's Environmental Health Basics for Early Intervention and Infant Development" toolkit was developed by the University of California, Davis Children's Center to serve as a template for future

outreach and education workshops. This toolkit was designed to help organize workshops for early intervention service providers and other infant development professionals seeking to increase their knowledge in environmental risks to neurodevelopment. The workshop template contains information that is easily modified to fit the varying requirements for different child development professional training conferences. Contents of the toolkit include workshop proposal, session outline and learning objectives (2-hour workshop), slide deck (including text, copyright-free images, imbedded videos), break-out activities and discussion guides, handouts (glossary, resources), and pre- and post-workshop assessments.

Science Sessions

The afternoon of Day 2 included research findings from the Children's Centers on the effects of environmental exposures and social stressors on children's health outcomes, including obesity, asthma, low birth weight, preterm birth, immune function, and the microbiome. Short summaries of these presentations have been included below. These abstracts reflect the individual views of meeting participants and centers, none of the statements represent analyses by or positions of EPA.

Obesity

Moderator: Dr. Frederica Perera, Ph.D., Dr.P.H., Columbia University

(1) Does Air Pollution Cause Childhood Obesity and Increased Risk for Diabetes? | *Rob McConnell, M.D., University of Southern California*
(2) Prenatal Phthalate Exposure and Metabolic Risk in Adolescence: Insights from metabolomics | *Karen Peterson, Sc.D., University of Michigan*
(3) Obesity as a Susceptibility Factor for Pollution Exposure and Lung Disease | *Meredith McCormick, M.D., M.H.S., Johns Hopkins University*

(1) Does Air Pollution Cause Childhood Obesity and Increased Risk for Diabetes?

Rob McConnell, M.D., University of Southern California

This presentation explored results related to air pollution, childhood obesity, and diabetes. The University of Southern California Children's Center is studying the effects of exposures to regional air pollutants and near-roadway air pollution on weight and diabetes risk in children. Results show that markers for near-roadway air pollution were associated with BMI in both boys and girls. Results also show synergistic associations of secondhand smoke and near-roadway air pollution exposure with BMI in children. There is compelling evidence that particulate matter exposure causes diabetes in animal studies and emerging evidence shows robust associations in adult epidemiological studies, but evidence that the risk is increased in children has not been well studied. To fill this research gap, center investigators examined associations of NO_2 and $PM_{2.5}$ with insulin sensitivity, acute insulin response to glucose, and disposition index in obese children and adolescents. Exposures to NO_2 and $PM_{2.5}$ were associated with long-term declines in insulin sensitivity and declines in disposition index (β-cell function). Exposure to $PM_{2.5}$ was also associated with increased acute response to glucose at age 18 years. These results have a potentially large public health impact. Possible interventions to lessen this impact include reducing levels of air pollution or mitigating effects of near-roadway air pollution through local zoning authority.

(2) Prenatal Phthalate Exposure and Metabolic Risk in Adolescence: Insights from metabolomics

Karen Peterson, Sc.D., University of Michigan

The presentation began by explaining the relationship between phthalates and metabolomics. The University of Michigan Children's Center examined whether trimester-specific exposures to phthalates are associated with metabolomics biomarkers among peripubertal youth. This is the first human study relating untargeted metabolomics during adolescence to *in utero* exposure to phthalates. Participants are part of the ELEMENT longitudinal birth cohort study in Mexico City. Researchers measured nine phthalates in maternal urinary samples from each trimester. A mass-spectrometry-based untargeted metabolomics platform was used to measure fasting serum metabolites in the children (ages 8-14 years), yielding data on hundreds of known and unknown chemical features. Researchers estimated the associations between each urinary phthalate and each serum metabolite, stratified by sex and adjusted for child age, BMI z-score, and pubertal onset. Accounting for multiple comparisons using a 10 percent false discovery rate ($q<0.1$), first trimester phthalates were not associated with any metabolites in the children. However, exposures during the second and third trimesters were significantly associated with sets of metabolites with the most associations observed among girls. Overall, metabolomics biomarkers may reflect sex differences in response to *in utero* phthalate exposures manifested during puberty that are not detected in clinical markers of cardiometabolic risk. The center plans to further explore how these metabolomic biomarkers relate to health outcomes, such as obesity and pubertal transition, among the children.

(3) Obesity as a Susceptibility Factor for Pollution Exposure and Lung Disease

Meredith McCormick, M.D., M.H.S., Johns Hopkins University

The Johns Hopkins University Children's Center studies how obesity and diet affect the relationship between indoor air pollution and asthma. Previous studies have shown that children who are obese or overweight have increased asthma symptoms in response to NO_2 and coarse particulate matter (PM_{10}). There is also an increased risk of doctor-diagnosed asthma in response to sulfur dioxide (SO_2) and PM_{10}. Obesity may alter the asthmatic response to ozone, and may also increase susceptibility to secondhand smoke. Diet was found to affect asthma symptoms independent of body mass. A Western diet has been associated with increased risk of wheeze, cough, and phlegm compared to consumption of a prudent diet. Researchers at Johns Hopkins University are conducting a study to further characterize the differential susceptibility to air pollution between overweight and obese children compared to non-obese children with asthma. Using an air purifier intervention study design, investigators are examining the effects of reduced PM exposure on asthma symptoms in obese versus non-obese children. They are also identifying potential mediators of susceptibility, including differences in breathing patterns, inflammatory and oxidative stress responses, and sleep-disordered breathing.

Cumulative Exposures and Stress

Moderator: Tracey Woodruff, Ph.D., University of California, San Francisco

(4) Assessing the Combined Effects of Environmental and Social Stress: A review of the evidence and implications for future research | *Rachel Morello-Frosch, Ph.D., M.P.H., University of California, Berkeley*

(5) Studying the Impacts of Environmental Exposures and Stress in the Puerto Rico CRECE Study | *John Meeker, Sc.D., M.S., University of Michigan*

(4) Assessing the Combined Effects of Environmental and Social Stress: A review of the evidence and implications for future research

Rachel Morello-Frosch, Ph.D., M.P.H., University of California, Berkeley

Researchers and communities have become increasingly concerned that variation in chemical exposures, social vulnerabilities, and biological susceptibility contribute to disparities in mortality and morbidity. The University of California, San Francisco Children's Center conducted a systematic review of the toxicology and epidemiological evidence on the combined effects of prenatal exposure to environmental chemicals and stress on fetal growth and other developmental outcomes. Most of the studies identified during the systemic review focused on tobacco smoke and air pollution. A meta-analysis of smoking studies evaluating interactive effects between maternal smoking and socioeconomic status (SES) found that the odds of low birthweight were significantly higher in low SES groups compared to high SES groups, indicating likely combined effects of chemical and psychosocial stressors. Very few human studies exist on other prenatal chemical exposures, such as endocrine disrupting chemicals, and their combined impacts with psychosocial stress. It is important to holistically measure stress in research, including place-based factors, individual measures, perceptual measures, and biomarkers. Findings related to cumulative impacts indicate that community engagement is essential in development of decision-making tools. As community engagement increases, residents become a more integral part of the research agenda and policy solutions to advance environmental health.

(5) Studying the Impacts of Environmental Exposures and Stress in the Puerto Rico CRECE Study

John Meeker, Sc.D., M.S., University of Michigan

The Northeastern University Children's Center is testing the modifying effects of SES, maternal stress, and preterm birth on the relationship between environmental phenols or parabens on pregnancy outcomes and child development. The CRECE study builds on the previously-established PROTECT pregnancy cohort in Puerto Rico and observes children born to mothers in the study. Researchers collect data, including biological and environmental samples, information on product use, geographical coordinates, and food frequency questionnaires, from mothers starting early in their pregnancy and continuing until they give birth. Researchers continue to collect data on the children until age four years. Preliminary analyses show that prenatal exposure to triclocarban resulted in almost two days-shorter gestational age. Researchers also collected data on maternal stress, then measured the interactive effect with phenols and parabens on children's health. This center will continue to interpret these analyses and study the combined effects of chemical and psychosocial factors.

Immune Function and the Microbiome

Moderator: Catherine Metayer, M.D., Ph.D., University of California, Berkeley

(6) Immune Dysregulation in Autism Spectrum Disorder | *Judy Van de Water, Ph.D., University of California, Davis*

(7) In Utero and Infant Arsenic Exposure, Immunity and the Microbiome: Results from the New Hampshire Birth Cohort Study | *Juliette Madan, M.D., Dartmouth College*

(8) Intergenerational Transmission of Risk: How the Microbiome Gets Under the Skin* | *Anne Dunlop, M.D., M.P.H., Michelle Wright, Ph.D., R.N., Emory University*

(6) Immune Dysregulation in Autism Spectrum Disorder

Judy Van de Water, Ph.D., M.D., University of California, Davis

The University of California, Davis Children's Center examines the roles of environmental factors, genes, and the immune system as they relate to autism spectrum disorder (ASD) susceptibility. They also explore the gestational immune environment in ASD. Disrupted maternal immune function may be a key factor in the later appearance of certain neurodevelopmental disorders. For example, a viral infection in early life may increase the risk of autism. Researchers measured maternal cytokines mid-gestation in the Early Markers of Autism (EMA) study – a case-control prospective study. Results show that mothers of children with ASD had elevated inflammatory cytokines and chemokines, which are normally downregulated during mid-gestation. These results suggest atypical immune regulation during pregnancy. A previously unidentified subtype of autism, Maternal Antibody Related (MAR) Autism, may be a result of maternal autoantibodies that cross the placenta and bind to their targets in the developing brain. These autoantibodies change how neurons develop. MAR cases make up about 20 percent of all ASD cases, and children with MAR autism exhibit more severe behaviors and pronounced stereotypic behavior. There are multiple points during development at which the environment can alter neurodevelopment. The environment can affect gestational development and interfere with neuroimmune interaction, as seen in MAR autism. The environment can also affect brain and immune system development after birth. Children with ASD also respond differently to toxicant exposures. For example, T cell cytokine production negatively correlates with total PBDE body burden in children with ASD. This response is opposite that of neurotypical children. Exploring differential immune sensitivity to various environmental exposures could provide clues as to the relationship between immune dysregulation and outcome in ASD.

(7) *In Utero* and Infant Arsenic Exposure, Immunity and the Microbiome: Results from the New Hampshire Birth Cohort Study

Juliette Madan, M.D., Dartmouth College

The Dartmouth College Children's Center studies early life exposure to arsenic, immunity, and the microbiome. The gut microbiome is essential in training the immune system early in life. Toxicants like arsenic have an antibiotic effect on the microbiome. Antibiotics reduce diversity during a critical window of metabolic development, and can impact overall health. For example, the proposed pathway in allergy, asthma, and autoimmune disease is that antibiotics eradicate diversity during critical windows of immune development. The center is working to determine how maternal gut, vaginal, and breast milk microbiomes affect the infant microbiome and gut metabolomics. In the New Hampshire Birth Cohort Study, researchers seek to investigate water and dietary sources of arsenic in regions with high well-water arsenic concentrations. Researchers follow children from birth and collect information about diet and biological samples (urine, breast milk) until age 5 years. Results show that delivery mode has the most substantial impact on infant gut microbiome. Results also show that the microbiome of children who were fed a mixed diet of formula and breast milk closely mirrors that of children who were exclusively formula fed. In addition to drinking water, the center also looks at the potential exposure to arsenic through food. Rice-based products are a food typically high in arsenic, which is of concern because over 80 percent of infants are introduced to rice cereal in the first year of life. Impacts of arsenic may occur at lower concentrations than previously known. Results show dose-related trends in risk of infection and wheeze, with no evidence of a lower threshold. The center plans to continue investigating the gut microbiome as a mediator of nutrition-infection associations.

(8) Intergenerational Transmission of Risk: How the Microbiome Gets Under the Skin

Anne Dunlop, M.D., M.P.H., Michelle Wright, Ph.D., R.N., Emory University

The transfer of microbes from mother and newborn starts before birth. The mode of delivery (vaginal versus Cesarean) and diet (breast milk versus formula) can also affect the infant microbiome. Changes in the maternal microbiome, preconception and during pregnancy, may initiate a transgenerational cycle of obesity. Maternal gut dysbiosis may be directly transmitted to the infant and cause dysbiosis. External influences such as early-life nutrition, mode of delivery, and antibiotic treatment may also influence the composition of the infant gut microbiome. These changes in gut microbiome function may result in infants being born large for gestational age with excess adiposity, both of which place the child at increased risk of obesity and immune dysfunction later in life. Adulthood obesity during childbearing years may perpetuate the cycle of obesity. With increasing prevalence of complex chronic disease in children, there has been an emerging focus on the contributions of early life exposures that lead to chronic health outcomes. Especially important is the concept of the exposome. Utilization of biological samples to study the exposome will encourage the discovery of alterations that represent how the exposome "gets under the skin" and contributes to health outcomes. The relationship between the maternal exposome and health outcomes of the offspring is complex. The presentation included a model to describe how the preconception and pregnancy exposome can contribute to high-risk birth outcomes and increased vulnerability to disease in the offspring throughout the life course. The presenters described how the fetal system responds through biologically mediated mechanisms to maternal exposures that potentially prime the body to anticipate similar exposures after birth. While these adaptations may provide short-term gains, they may also have negative consequences later in life that contribute to adult disease. Epigenetic mechanisms, such as DNA methylation, contribute to the development of certain observable characteristics. In addition to the influence of nutrients and diet, the microbiome can result in changes to DNA methylation and influence fetal health.

Keynote

Science to Policy: Incorporating Children's Health into Decision-Making

Gina M. Solomon, M.D., M.P.H., Deputy Secretary for Science and Health, California Environmental Protection Agency

Dr. Solomon began her presentation by discussing the overall mission and activities of the California Environmental Protection Agency (CalEPA). She then described the specific role CalEPA serves in protecting children's health. In 1999, the California legislature created the Children's Environmental Health Center within CalEPA. The CalEPA Center reviews ambient air quality standards to ensure that they protect infants and children, establishes a list of toxic air contaminants that may disproportionality affect children, and revises control measures for these contaminants. Dr. Solomon noted that children face cumulative stressors, including environmental hazards and social factors, intrinsic biological and physiological factors, as well as external social vulnerability factors. She then expanded on how these stressors modify the effects of environmental hazards on children's health and expressed the importance and value of tools and analytical methods that can accurately assess cumulative stressors. Dr. Solomon described one such tool, CalEnviroScreen 3.0, which was released in January 2017. CalEnviroScreen, available online, conducts spatial analysis of relative burdens from pollution and population vulnerability in California communities. The tool combines 20 different indicators into a single score. These indicators measure both pollution burden and population characteristics. The final CalEnviroScreen score allows for comparison of different geographical areas.

Higher scores mean greater pollution burdens and population vulnerability. Dr. Solomon proceeded to discuss other efforts by CalEPA, including those focused on investing in and funding projects in disadvantaged communities. Another CalEPA project identifies gaps in chemicals policy. For example, the California Safer Consumer Products Program, passed by California legislature in 2008, selects products and chemicals that may cause harm to human health, evaluates alternatives, and considers possible responses. Products and chemicals are prioritized for action if there is potential for exposures to contribute to or cause significant or widespread adverse impacts. Dr. Solomon concluded her presentation by discussing future policy priorities for CalEPA and thanked the organizers for the opportunity to share the work of CalEPA.

Appendices

Appendix A – List of Participating Children's Centers

Columbia University – NIEHS/EPA Children's Environmental Health Centers; The Columbia Center for Children's Environmental Health (CCCEH)

Dartmouth College – NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers at Dartmouth College

Duke University – NIEHS/EPA Children's Environmental Health Centers Center for Study of Neurodevelopment and Improving Children's Health Following Environmental Tobacco Smoke Exposure (NICHES)

Emory University – NIEHS/EPA Children's Environmental Health Centers Center for Children's Health, the Environment, the Microbiome and Metabolomics (C-CHEM^2)

Johns Hopkins University – NIEHS/EPA Children's Environmental Health Centers Center for the Study of Childhood Asthma in the Urban Environment (CCAUE)

Northeastern University – NIEHS/EPA Children's Environmental Health Centers Center for Research on Early Childhood Exposure and Development in Puerto Rico (CRECE)

University of California, Berkeley CERCH – NIEHS/EPA Children's Environmental Health Centers Center for Environmental Research and Children's Health (CERCH)

University of California, Berkeley CIRCLE – NIEHS/EPA Children's Environmental Health Centers Center for Integrative Research on Childhood Leukemia and the Environment (CIRCLE)

University of California, Berkeley/Stanford University (CHAPS) – NIEHS/EPA Children's Environmental Health Centers Children's Health and Air Pollution Study – San Joaquin Valley (CHAPS – SJV)

University of California, Davis – NIEHS/EPA Children's Environmental Health Centers UC Davis Center for Children's Environmental Health and Disease Prevention

University of California, San Francisco – NIEHS/EPA Children's Environmental Health Centers: THE UCSF Pregnancy Exposures to Environmental Chemicals (PEEC) Children's Center

University of Illinois – NIEHS/EPA Children's Environmental Health Centers: Novel Methods to Assess Effects of Chemicals on Child Development

University of Michigan – NIEHS/EPA Children's Environmental Health Centers: Lifecourse Exposures & Diet: Epigenetics, Maturation & Metabolic Syndrome

University of Southern California – NIEHS/EPA Children's Environmental Health Centers: Southern California Children's Environmental Health Center

University of Washington – NIEHS/EPA Children's Environmental Health Centers Center for Child Environmental Health Risks Research

Appendix B – Meeting Agenda

NIEHS/EPA Children's Centers Annual Meeting
EPA Region 9, 75 Hawthorne Street, San Francisco, CA
October 24-25, 2017

Meeting Goals and Objectives:

- *The jointly-funded NIEHS/EPA Children's Centers Annual Meeting provides an opportunity to share the robust research and scientific analysis that is the foundation of the Children's Centers program. The 2017 meeting is hosted together with the Pediatric Environmental Health Specialty Units (PEHSUs).*
- *This meeting allows the Children's Centers and PEHSUs to form new collaborations with each other and with community, state, and federal partners to positively impact public health.*

Tuesday, Oct. 24, 2017

8:30 a.m. – 8:40 a.m.	**Conference Overview** Nica Louie, M.S., Project Officer, U.S. Environmental Protection Agency (EPA) Kimberly Gray, Ph.D., Health Science Administrator, National Institute of Environmental Health Sciences (NIEHS)
8:40 a.m. – 9:00 a.m.	**Welcoming Remarks** Alexis Strauss, M.A., Acting Regional Administrator, EPA Region 9 Gwen Collman, Ph.D., Director, Division of Extramural Research and Training, NIEHS Elaine Cohen Hubal, Ph.D., M.S., Office of Research and Development, EPA
9:00 a.m. – 10:15 a.m.	**Progress Review (Part I)** The Children's Centers and PEHSUs will present updates, recent successes, robust science and scientific analysis aimed at protecting the health of children. Five-minute presentations will be followed by ten-minute small group discussions. While this session includes seven posters, there is time for each participant to visit four posters. - Columbia University, *Longitudinal Effects of Prenatal Exposure to PAHs on Mental, Behavioral, and Emotional Disorders as well as Obesity in Adolescence* - Dartmouth College, *Should Rice Cereal be an Infant's First Food?* - Duke University, *Exposure to Tobacco Smoke During Pregnancy – and Even During Preconception – Can Alter Baby's Brain Function* - Emory University, *African American Women in Metro Atlanta Have Higher Levels of Endocrine Disrupting Plasticizers in Their Bodies Than Other African American Women* - Johns Hopkins University, *Obesity and Diet as Susceptibility Factors to Air Pollution Exposure*
10:15 a.m. – 10:30 a.m.	**Break**

10:30 a.m. – 11:30 a.m. **Quick Connections Round I**

Through a series of short conversations, participants will identify new potential collaborators to improve and protect public health. In addition to networking, participants will also share what makes them passionate about children's environmental health. Specific directions will be provided separately.

11:30 a.m. – 12:45 p.m. **Lunch** (on your own)

12:45 p.m. – 2:00 p.m. **Progress Review (Part II)**

The Children's Centers and PEHSUs will present updates, recent successes, robust science and scientific analysis aimed at protecting the health of children. Five-minute presentations will be followed by ten-minute small group discussions. While this session includes six posters, there is time for each participant to visit four posters.

- Northeastern University, *Exposure to triclosan in pregnancy is associated with increased inflammation*
- UC Berkeley (CERCH), *Mixtures of Pesticides Used Near Homes During Pregnancy Associated with Decreased IQ in Children*
- UC Berkeley (CIRCLE), *Toxic PCBs Still Harming Children, Despite Long-Time Ban*
- UC Berkeley/Stanford University, *Ambient Air Pollution Impairs Immune Function, which Impacts Allergy and Asthma*
- UC Davis, *Can Newborn Cytokines Predict Autism?*
- PEHSU Region 2, *Effectively Integrate Environmental Health into Clinical Practice*

2:00 p.m. – 3:00 p.m. **Quick Connections Round II**

Through a series of short conversations, participants will identify new potential collaborators to improve and protect public health. In addition to networking, participants will also share what makes them passionate about children's environmental health. Specific directions will be provided separately.

3:00 p.m. – 3:15 p.m. **Break**

3:15 p.m. – 4:30 p.m. **Progress Review (Part III)**

The Children's Centers and PEHSUs will present updates, recent successes, robust science and scientific analysis aimed at protecting the health of children. Five-minute presentations will be followed by ten-minute small group discussions. While this session includes six posters, there is time for each participant to visit four posters.

- UC San Francisco, *Flame Retardants Linked to Lower Child IQ*
- University of Illinois, *Through the Window of a Baby's Eyes*
- University of Michigan, *Toxicant Exposures and Lifestyle Factors Influence the Rate of Epigenetic Aging*
- University of Southern California, *Does Air Pollution Cause Childhood Obesity and Increase the Risk of Diabetes?*

- University of Washington, *Longitudinal Exposome Research Reveals Exposure of Agricultural Families to Over 86 Pesticides, 47 of Which May Impact Neurodevelopment in Young Children*
- PEHSU Region 9, *A Story of Health Multimedia eBook Improves Environmental Health Literacy of Thousands of Health Professionals*

4:30 p.m. **Adjourn**

Wednesday, Oct. 25, 2017

8:30 a.m. – 8:40 a.m. **Introduction**

8:40 a.m. – 12:05 p.m. **Lightning Talks**

The Children's Centers and PEHSUs will present communication tools and approaches that educate the community children's environmental health topics. The objective is to share tools and approaches that other centers and PEHSUs can adapt for their own communities.

Discussion Questions

1. Identify a partner/stakeholder who would find the tool useful or educational.
2. What is the best way to disseminate this tool/approach to its target audience?
3. What suggestions do you have that could improve this tool?
4. Do you have a similar or complimentary tool that you could make available to others – if so what?

8:40 a.m. – 9:45 a.m. **Session I – Tools Targeted to Pregnant Women and Parents**

- Emory University*, 'Know Better, Live Better' Social Media campaign*
- Columbia University, *Communication Tools for Parents and Caregivers*
- University of Washington, *Communicating with Parents and Community: Examples for explaining individual and population level pesticide exposures*
- UC San Francisco, *Toxic Matters*
- EPA*, Children's Centers Impact Report*

Moderator: Carmen Marsit, Ph.D., Emory University

9:55 a.m. – 10:55 a.m. **Session II – Tools Targeted to Children and Adolescents**

- UC Berkeley CIRCLE*, Improving Environmental Health Literacy of Adolescents and Young Adults: Research to Real Life*
- PEHSU Region 4, *Break the Cycle of Children's Environmental Health Disparities in Poor Communities*
- UC Berkeley CERCH, *Youth Participatory Action: A Tool for Community Communication*
- Emory University, *Empowering children through environmental health literacy: Moving Beyond Didactic Guest Lectures*

Moderator: Susan Murphy, Ph.D., Duke University

11:05 a.m. – 12:05 p.m. **Session III – Tools Targeted to Professionals (medical, childcare, schools)**

- University of Illinois*, Which Environment? Shifting Communication Strategies to Meet Child Care Provider Needs*
- Northeastern University, *Environmental Health Education for Health Professionals*
- University of Michigan*, Environmental Health Screening Tools to be Used by Head Start teachers*
- UC Davis*, Children's Environmental Health Basics for Early Intervention/Infant Development Professionals*

Moderator: Susan Buchanan, M.D., M.P.H., PEHSU Region 5

12:05 p.m. – 1:30 p.m. **Lunch** (on your own)

1:30 p.m. – 4:30 p.m. **Science Seminars**

This session provides an overview of environmental factors that may contribute to multiple health endpoints. The session includes presentations as well as panel discussions.

1:30 p.m. – 2:35 p.m. **Obesity**

1:30 p.m. – 1:35 p.m.	*Introduction*, Frederica Perera, Ph.D., Columbia University
1:35 p.m. – 1:50 p.m.	*Does Air Pollution Cause Childhood Obesity and Increased Risk for Diabetes*, Rob McConnell, M.D., University of Southern California
1:50 p.m. – 2:05 p.m.	*Prenatal Phthalate Exposure and Metabolic Risk in Adolescence: Insights from Metabolomics*, Karen Peterson, Sc.D., University of Michigan
2:05 p.m. – 2:20 p.m.	*Obesity as a Susceptibility Factor for Pollution Exposure and Lung Disease*, Meredith McCormack, M.D., M.H.S., Johns Hopkins University
2:20 p.m. – 2:35 p.m.	Discussion

2:35 p.m. – 3:25 p.m. **Cumulative Exposures and Stress**

2:35 p.m. – 2:40 p.m.	*Introduction*, Tracey Woodruff, Ph.D., M.P.H., UC San Francisco
2:40 p.m. – 2:55 p.m.	*Cumulative Prenatal Exposure to Exogenous Chemicals and Psychosocial Stress: A review of the evidence and implications for future research*, Rachel Morello-Frosch, Ph.D., M.P.H., UC Berkeley
2:55 p.m. – 3:10 p.m.	*Studying the Impacts of Environmental Exposures and Stress in the Puerto Rico CRECE study*, John Meeker, Sc.D., M.S., University of Michigan
3:10 p.m. – 3:25 p.m.	Discussion

3:25 p.m. – 4:30 p.m. **Immune Function and the Microbiome**

	3:25 p.m. – 3:30 p.m.	*Introduction*, Catherine Metayer, M.D., Ph.D., UC Berkeley
	3:30 p.m. – 3:45 p.m.	*Immune Dysregulation in Autism Spectrum Disorder*, Judy Van de Water, Ph.D., UC Davis
	3:45 p.m. – 4:00 p.m.	*In Utero and Infant Arsenic Exposure, Immunity and the Microbiome: Results from the New Hampshire Birth Cohort Study*, Juliette Madan, M.D., Dartmouth College
	4:00 p.m. – 4:15 p.m.	*Intergenerational Transmission of Risk: How the Microbiome Gets Under the Skin*, Anne Dunlop, M.D., M.P.H., Emory University; Michelle Wright, Ph.D., R.N., Emory University
	4:15 p.m. – 4:30 p.m.	Discussion
4:30 p.m. – 5:00 p.m.	Keynote Gina Solomon, M.D., M.P.H., Deputy Secretary for Science and Health, California Environmental Protection Agency Moderator: Mark Miller, M.D., M.P.H., PEHSU Region 9	
5:00 p.m.	Adjourn	

Appendix C – List of Steering Committee Members

Hayley Aja, EPA Student Contractor

Laura Anderko, PEHSU Region 2

Akram Alshawabkeh, Northeastern University Children's Center

Martha Berger, EPA

Susan Buchanan, PEHSU Region 5

Annemarie Charlesworth, University of California, San Francisco Children's Center

Jose Cordero, Northeastern University Children's Center

Brenda Eskenazi, University of California, Berkeley CERCH Children's Center

Michael Firestone, EPA

Kenda Freeman, NIEHS

Andrew Geller, EPA

Kimberly Gray, NIEHS

Virginia Guidry, NIEHS

S. Katharine Hammond, University of California, Berkeley/Stanford University Children's Center

Kim Harley, University of California, Berkeley CERCH Children's Center

Elaine Cohen Hubal, EPA

Pam Lein, University of California, Davis Children's Center

Nica Louie, EPA

Carmen Marsit, Dartmouth College Children's Center

Rob McConnell, University of Southern California Children's Center

Jacquelyn Menghrajani, EPA Region 9

Catherine Metayer, University of California, Berkeley CIRLCE Children's Center

Mark Miller, PEHSU Region 9, University of California, Berkeley CIRCLE Children's Center

Susan Murphy, Duke University Children's Center

Birgit Puschner, University of California, Davis Children's Center

Perry Sheffield, PEHSU Region 2

Emily Szwiec, ASPPH

Kelly Widener, EPA

Nsedu Obot Witherspoon, Children's Environmental Health Network

Tracey Woodruff, University of California, San Francisco Children's Center

Appendix D – List of Participants

The 2017 Children's Centers Annual Meeting included 116 total participants, including center researchers, PEHSUs, EPA labs and centers, EPA regional offices, NIEHS, and CDC.

Angeles Acosta Rodriguez, University of Puerto Rico/Northeastern University

Andrea Aguilar, University of Illinois

Marcus Aguilar, EPA Region 9

Hayley Aja, EPA

Akram Alshawabkeh, Northeastern University

John Balmes, University of California, San Francisco

Jacqueline Barkoski, University of California, Davis

Kim Bartels, EPA Region 8

Martha Berger, EPA

Cassie Bernardi, American Academy of Pediatrics

Stephen Borron, PEHSU Region 6

Asa Bradman, University of California, Berkeley

Susan Buchanan, PEHSU Region 5

Kimberly Burke, Columbia University

Rich Campbell, EPA

Annemarie Charlesworth, University of California, San Francisco

Elaine Cohen Hubal, EPA

Jose Cordero, University of Georgia

Mona Dai, EPA

Natalyn Daniels, University of California, San Francisco

Dana Dolinoy, University of Michigan

Christie Drew, NIEHS

Anne Dunlop, Emory University

Brenda Eskenazi, University of California, Berkeley

Elaine Faustman, University of Washington

Bryan Fiedorczyk, EPA Region 10

Barbara Fiese, University of Illinois

Jill Franzosa, EPA

Bernard Fuemmeler, Virginia Commonwealth University

Sam Goldman, University of California, San Francisco

Jackie Goodrich, University of Michigan

Robert Gould, University of California, San Francisco

Kimberly Gray, NIEHS

Wendy Gutschow, University of Southern California

Angela Hackel, EPA

Katharine Hammond, University of California, Berkeley

Nadia Hansel, Johns Hopkins University

Kim Harley, University of California, Berkeley

Michael Hatcher, Centers for Disease Control (CDC), Agency for Toxic Substances and Disease Registry (ATSDR)

Marissa Hauptman, PEHSU Region 1

Irva Hertz-Picciotto, University of California, Davis

Stephanie Holm, PEHSU Region 9

Karen Huen, University of California, Berkeley

Gredia Huerta-Montanez, Northeastern University

Brenda Koester, University of Illinois

Susan Korrick, Harvard University

Patricia Lasley, PEHSU Region 5

Chris Lau, EPA

Robin Lee, University of Michigan

Victoria Leonard, University of California, San Francisco

Edward Levin, Duke University

Sa Liu, University of California, Berkeley

Nica Louie, EPA

Jennifer Lowry, PEHSU Region 7

Fred Lurmann, Sonoma Technology Inc.

Lisa Lutzker, University of California, Berkeley

Juliette Madan, Dartmouth College

Ehsan Majd, Johns Hopkins University

Melinda Malamoco, PEHSU Region 8

Jennifer Mann, University of California, Berkeley

Carmen Marsit, Emory University

Linda McCauley, Emory University

Rob McConnell, University of Southern California

Meredith McCormack, Johns Hopkins University

John Meeker, University of Michigan

Jaquelyn Menghrajani, EPA Region 9

Mark Miller, University of California, San Francisco

Rachel Morello-Frosch, University of California, Berkeley

Susan Murphy, Duke University

Carolyn Murray, Dartmouth College

Nathan Mutic, Emory University

Abby Mutic, Emory University

Kari Nadeau, Stanford University

Andreas Neophytou, University of California, Berkeley

James Nolan, University of California, Berkeley

Elizabeth Noth, University of California, Berkeley

Liam O'Fallon, NIEHS

Vasantha Padmanabhan, University of Michigan

Amy Padula, University of California, San Francisco

Frederica Perera, Columbia University

Karen Peterson, University of Michigan

Lillian Prince, University of California, San Francisco

Kenisha Puckett, University of California, San Francisco

Danielle Ramos, ASPPH, EPA

Cynthia Rand, Johns Hopkins University

Virginia Rauh, Columbia University

Jamie Rayman, CDC, ATSDR

John Rodgers, EPA

Jeannie Rodriguez, Emory University

Melissa Rose, University of California, Davis

P. Barry Ryan, Emory University

Sheela Sathyanarayana, Seattle Children's Research Institute

Vicki Sayarath, Dartmouth College

Susan Schantz, University of Illinois

Rebecca Schmidt, University of California, Davis

Sophia Serda, EPA Region 9

Sarah Sharpe, University of California, Berkeley

Perry Sheffield, Icahn School of Medicine at Mount Sinai, PEHSU Region 2

Veena Singla, University of California, San Francisco

Gina Solomon, California Environmental Protection Agency

Gretchen Stewart, EPA Region 10

Patrice Sutton, University of California, San Francisco

Emily Szwiec, ASPPH, EPA

Claudia Thompson, NIEHS

Gwen Tindula, University of California, Berkeley

Judy Van de Water, University of California, Davis

Julia Varshavsky, University of California, San Francisco

Julia Vassey, University of California, Berkeley

Carmen Velez Vega, University of Puerto Rico/Northeastern University

Aolin Wang, University of California, San Francisco

Lois Wessel, Georgetown University

Todd Whitehead, University of California, Berkeley

Siobhan Whitlock, EPA Region 4

Patrick Wilson, EPA Region 9

Tracey Woodruff, University of California, San Francisco

Michelle Wright, Emory University

Marya Zlatnik, University of California, San Francisco

Appendix E – Progress Update Poster Presentations

The views expressed in these presentations are those of the authors and do not necessarily represent the views or policies of EPA.

COLUMBIA CENTER FOR CHILDREN'S ENVIRONMENTAL HEALTH

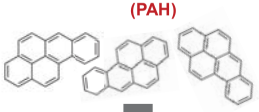
MAILMAN SCHOOL OF PUBLIC HEALTH
COLUMBIA UNIVERSITY

Longitudinal Effects of Prenatal Exposure to Polycyclic Aromatic Hydrocarbons (PAH) on Mental, Behavioural, and Emotional Disorders as well as Obesity in Adolescence

THE COLUMBIA CENTER FOR CHILDREN'S ENVIRONMENTAL HEALTH (CCCEH):
Selected Accomplishments from 2016-17

HYPOTHESIS

Polycyclic Aromatic Hydrocarbons (PAH)



Neurotoxic pollutants released from fossil fuels, tobacco, and other organic material

Prenatal and Early Childhood Exposure

Disrupts Development and Maturation of Neural Systems that Support Capacities for **Self-Regulation**

Vulnerable Period of Adolescence

Cognitive, Emotional, Behavioural, and Adiposity Problems

SPECIFIC AIMS

Elevated prenatal PAH exposure is associated with:

1) Adverse effects on self-regulatory processes and clinical symptoms at age 15-17 years, and distinctive adverse developmental trajectories from early childhood through age 15-17 years of age
2) Distinct growth trajectories of body mass index growth and fat mass index from age 5 to17 years, and greater adiposity, higher hedonic eating behavior, sedentary pursuits, and poorer neuropsychological function at age 15-17 years of age
3) Adverse effects on the structure, function, and metabolism of neural systems known to support the capacity for self-regulation at 9-12 years (visualized by MRI), which mediate the emergence of conduct disturbance, substance use, depression, the persistence of ADHD symptoms, and adiposity measures up to 15-17 years of age

KEY RESEARCH FINDINGS

Longitudinal effects of prenatal exposure to air pollutants on self-regulatory capacities and social competence

Margolis et al, 2016

POPULATION

- **Recruited from 1998-2006**
- **African-American and Dominican women residing in Harlem, South Bronx, and Washington Heights, NY**
- **Non-active cigarette smokers, ages 18-35 years, non users of other tobacco products or illicit drugs, free of diabetes, hypertension, or known HIV**

MEASURES

Deficient Emotional Self Regulation (DESR) examines:
- **Anxiety/Depressed**
- **Aggressive Behavior**
- **Attention Problems**

Assessed for children at 3-5, 7, 9, and 11 years of age.

Social Responsiveness Scale (SRS) examines:
- **Social Awareness**
- **Social Cognition**
- **Social Communication**
- **Social Motivation**
- **Autistic Mannerisms**

Assessed for children 11 years of age.

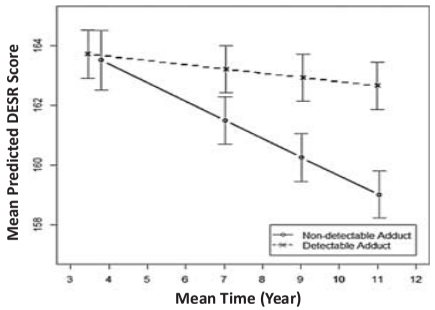
Key Research Finding A

The effects of adducts on DESR were not constant over time (p = 0.05)
- Among those **without detectable adducts**, the average DESR score decreased substantially over time (**-0.38% per year**)
- Among those **with detectable adducts**, average DESR score decreases minimally over time (**-0.09% per year**)

Implication

Developmental trajectory of self-regulatory capacity was delayed in children exposed to PAH.

n = 462



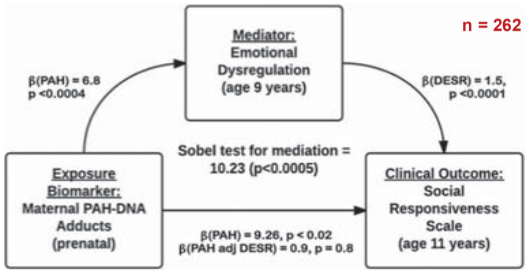
Key Research Finding B

- Positive association between presence of **PAH-DNA adducts** and **problems with social competence** (p < 0.04)
- Positive association between **level of dysregulation** and **problems with social competence** (p < 0.0001)
- Evidence that **self-regulation mediates the association** of prenatal exposure to PAH with social competence (p < 0.0007)

Implication

Deficits in self-regulatory capacities across early and middle childhood lead to emerging social problems with real-world consequences for high-risk adolescent behaviours in this minority urban cohort.

n = 262



PRELIMINARY FINDINGS

Combined Effects of Prenatal Exposure to Polycyclic Aromatic Hydrocarbons and Material Hardship on Child ADHD Behavior Problems

Perera et al, 2017

ADHD symptoms	Estimate	95% CI	p value
ADHD analyzed continuously			
ADHD Index	0.42	0.11-0.74	0.01
DSM-IV Inattentive	0.46	0.13-0.79	0.01
DSM-IV Hyperactive-Impulsive	0.33	0.03-0.62	0.03
DSM-IV Index Total	0.39	0.10-0.68	0.01
ADHD analyzed dichotomously			
ADHD Index	1.23	0.12-2.35	0.03
DSM-IV Inattentive	1.77	0.62-2.93	<0.01
DSM-IV Hyperactive-Impulsive	0.50	-0.61-1.61	0.38
DSM-IV Index Total	1.40	0.35-2.46	0.01

Co-exposure to socioeconomic disadvantage (lack of adequate food, housing, utilities, and clothing) and prenatal PAH significantly increases the risk of ADHD behaviour problems, particularly high PAH and persistent hardship (see table above).

CHALLENGES

We experienced **delays in participant recruitment** and the rate of assessment due to the need to refine the MRI protocol for imaging the brain and abdomen in the same MRI visit.

Solution

By **scheduling more visits during the summer months and weekends**, we are on target to achieve our goals.

ACKNOWLEDGEMENTS

Funding was provided by the National Institute for Environmental Health Sciences (**NIEHS**) and the U.S. Environmental Protection Agency (**US EPA**): NIEHS/EPA P50 ES009600-18.

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Should Rice Cereal be an Infant's First Food?

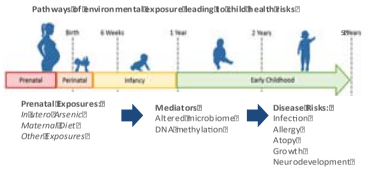
THE CHILDREN'S ENVIRONMENTAL HEALTH & DISEASE PREVENTION RESEARCH CENTER AT DARTMOUTH

Carolyn Murray, MD, MPH, Juliette Madan, MD, MS, Kathy Cottingham, MS, PhD, Carol Folt, PhD, Diane Gilbert-Diamond, ScD, Brian Jackson, PhD, Susan Korrick, MD, MPH, Carmen Marsit, PhD, John Moeschler, MD, Kari Nadeau, MD, PhD, Tracy Punshon, PhD, David Robbins, PhD, Vicki Sayarath, MPH, RD, and Margaret Karagas, MS, PhD

The New Hampshire Birth Cohort Study

Specific Aims

- The primary aims of our Center are to identify exposure to common environmental contaminants such as arsenic during fetal development and childhood; the impact these exposures have on childhood immunity, growth, and neurological development and the mechanisms by which they may be operating. We also are are committed to sharing these findings with key stakeholders which include parents, pediatric health care providers, policy makers and communities.



NEW HAMPSHIRE BIRTH COHORT STUDY

Formative Phase	1st Follow-up Phase	2nd Follow-up Phase

Pregnancy → Delivery → Months 4-8-12 → >1 Years

Pregnancy

12-16 Weeks
- *Eligibility screen*

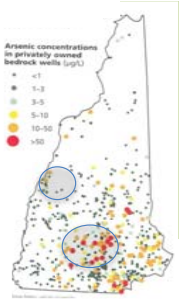
24-28 Weeks
- Questionnaire
- Maternal blood, urine, hair, toenail, tap water
- Maternal diet (FFQ, diary)
- Prenatal records, including maternal infection, ultrasounds

Delivery — NHBCS
- Birth Outcomes
- Maternal/infant health status
- Cord blood
- Placenta
- Meconium/transition stool (microbiome, metabolmics)
- NNNS

Months 4-8-12 — NHBCS
- Child exposures, health/respiratory & growth
- Infant & maternal diet (FFQ, diary)
- Breast milk
- Infant nails/urine/stool/blood (metals/microbiome /metabolomics)
- Vaccine response
- Pediatric record review

>1 Years — NHBCS
- Child exposures, health/respiratory & growth
- Child diet (FFQ/diary, 3 & 5 y)
- Child blood/urine/ stool
- Neurodevelopment (3 & 5 y)
- Anthropometry, BP (5 y)
- Pediatric record review

- **Cohort Location:** 2 regions of rural New Hampshire
- **Inclusion Criteria:**
  - Pregnant women, ages 18-45 years old;
  - Receiving OB care at prenatal clinics;
  - Household served by a private water system;
  - No plans for moving prior to delivery;
  - Singleton pregnancy;
  - English speaking, literate, mentally competent.
- **Subject Recruitment:** Eligible women recruited at ~24-28 wks gestation NHBCS; 12 wks gestation ECHO
- **Year recruitment began: January** 2009
- **Participants recruited to date:** 1,741; goal 3,000
- **Age of oldest children:** 8 years

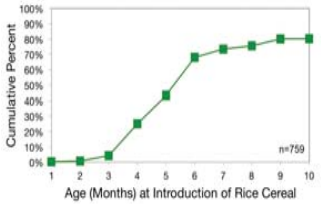


Findings

Exposures

- Urinary arsenic (As) concentrations during pregnancy relate to both water As & rice intake (Gilbert-Diamond, *PNAS*, 2011)
- Maternal rice intake related to infant As biomarker concentrations (Davis, *JESEE*, 2014)
- 80% of infants introduced to rice cereal in 1st yr of life (Karagas, *JAMA Peds*, 2016)
- Breast milk low in As, & breast fed infants had lower urinary As than formula fed infants (Carignan, *EHP*, 2015)

Infants' Rice Cereal Introduction



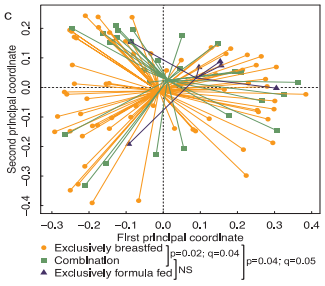
Translation

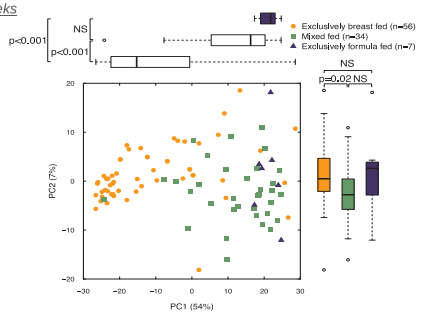
- *New results from work of our COTC indicate that women who receive results of elevated well water arsenic levels report less use of their tap water for drinking, cooking, and for mixing infant formula than women who received reports of low or no arsenic in their well water.*

Mediators

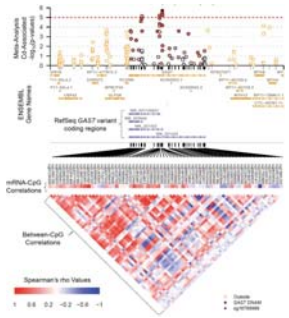
- Infant microbiome associated with feeding mode (breast feeding, formula feeding and mixed feeding) (Madan, *JAMA Peds*, 2016)
- *Preliminary data on infant fecal metabolomics profiles indicate differences by feeding mode (breast milk vs. formula) (Hoen, Unpublished)*

Diet during first 6 weeks





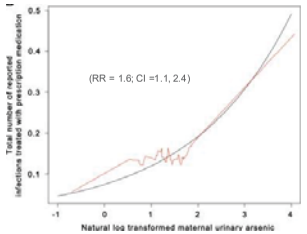
- Placental epigenetic and gene expression alterations act as functional mediators of maternal toxic metals exposure on newborn outcomes (Green *EHP* 2016; Everson *Envir Res* 2017; Winterbottom *EH* 2017; Appleton *Epigenetics* 2017; Everson *Repro Tox* 2016; Winterbottom *EBioMedicine* 2015)



Outcomes

- Maternal arsenic exposure is related to heightened risk of respiratory symptoms and infection in infants' first year of life (Farzan, 2013; Farzan, *EH*, 2016; Farzan, 2017).

Arsenic exposure and infection



Successes & Challenges

- **NHBCS:**
  - Successfully engaged prenatal clinics & hospitals; recruited maternal-infant dyads; collected environmental and biologic samples, questionnaire data and assessments; and published impactful results on maternal-child health;
  - Use of a rural population for critical exposure – mediation – outcome assessment.

COTC:
- Effectively communicating our findings about arsenic in food and water to relevant stakeholders presented challenges, particularly as we sought to avoid unintended consequences, such as inappropriate dietary changes.
- To address these challenges we:
  - held focus groups with NHBCS participants
  - produced interactive web-tools for parents to explain sources of arsenic and ways to avoid them
  - met with federal agencies and congressional offices, and testified at an FDA food policy committee
  - organized an interdisciplinary collaborative and published scientific reports to reach both the scientific and medical community to inform ways to reduce children's exposure to dietary arsenic.

FDA

GAO Accountability * Integrity * Reliability

ConsumersUnion®

C-FARR Collaborative on Food with Arsenic and associated Risk and Regulation

United States Representative ROSA DELAURO Representing the 3rd District of Connecticut

Exposure To Tobacco During Pregnancy – and Even Preconception – Can Alter Offspring's Brain Function

Theodore A Slotkin, Ashley Stadler, Samantha Skavicus, Jennifer Card, Jonathan Ruff, Brandon J Hall, Yael Abreu-Villaca, Shaqif Junaid, Hannah White, Aptin Kiany, Lisa Guo, Zhiqing Huang, Frederic J Seidler and Edward D Levin

Presenter: Susan K Murphy

Overall Specific Aims

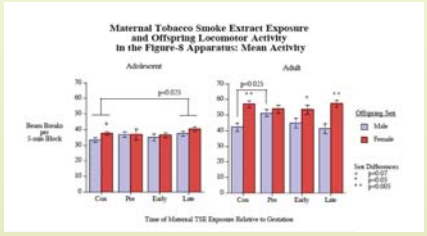
Aim 1: To define relevant epigenomic-transcriptomic changes induced by nicotine exposure.

Aim 2: Examine the effect of exposure timing on outcome and epigenetic effects.

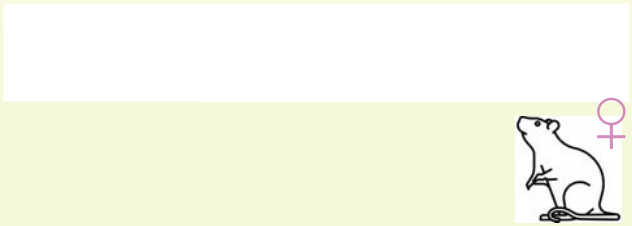
Aim 3: Determine if methylation mediates the relationship between environmental tobacco smoke exposure and ADHD-related neurobehaviors.

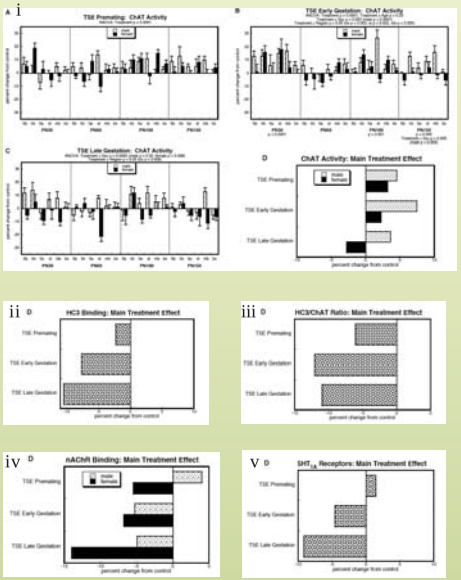
Aim 4: Train multidisciplinary researchers to impact environmental health sciences.

Research Findings



	Controls M v F	Pre v Controls M, M, F? (M v F)	Early v Controls M, F? (M v F)	Late v Controls M, F? (M v F)
Elevated Plus Maze (anxiety; time in open arms)	ns	ns (ns)	ns (ns)	p<0.05 M + F (ns)
Figure 8 Apparatus (activity-adolescent; beam breaks per 5 minutes)	p<0.07	ns (ns)	ns (ns)	p<0.025 M + F (ns)
Figure 8 Apparatus (activity-adult; beam breaks per 5 minutes)	p<0.005	p<0.025 M (ns)	ns (p<0.05)	ns (p<0.005)
Figure 8 Apparatus (habituation - adolescence; linear trend 5 min blocks)	ns	p<0.05 M + F (ns)	ns (ns)	ns (ns)
Figure 8 Apparatus (habituation - adult; linear trend 5 min blocks)	ns	ns (ns)	ns (ns)	ns (ns)
Radial Arm Maze (working memory errors, fed)	ns	p<0.05 M + F (ns)	ns (ns)	ns (ns)
Radial Arm Maze (working memory errors, restricted)	ns	ns (ns)	ns (ns)	ns (ns)
Radial Arm Maze (working memory errors, fed versus restricted)	p<0.005	ns	p<0.05	ns
Attention Task (hits)	ns	ns	p<0.025 M + F (ns)	p<0.05 M + F (ns)
Attention Task (correct rejection)	ns	ns	ns	ns





Acetylcholine and serotonin synaptic markers

- Original data shown in (i); collapsed data in (ii) through (vi).
- Frontal/parietal cortex (f/p), temporal/occipital cortex (t/o), midbrain (mb), brainstem (bs), hippocampus (hp), striatum (st)
- 1 male and 1 female used per litter

Preliminary Research Findings

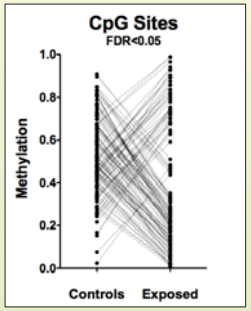
Tobacco Smoke Extract 0.2 mg/kg/day

14 days

Sperm N=12 per group

Reduced Representation Bisulfite Sequencing

Possibility of paternal transmission?



Chromosome: Nucleotide	Gene Symbol	Gene Name	FDR	Exposed vs. Controls
chr1:222417370 chr1:222417354	*Macrod 1*	*macro domain-containing 1*	0 0	7.3% -47.4%
chr5:173290694 chr5:173290712	*Mxra8*	*matrix remodeling associated 8*	6.3E-07 1.6E-04	-47.5% 1.0%
chr11:38457229	*Zfp295*	*zinc finger protein 295*	.4E-06	27.6%
chr18:24735001 chr18:24734964 chr18:24735036 chr18:24734922 chr18:24735041	*Lims2*	*LIM zinc finger domain containing 2*	1.2E-05 1.2E-05 1.2E-05 1.7E-04 .4E-04	-61.7% -62.1% -62.1% -58.0% -57.7%
chr5:118348170	*Foxd3*	*forkhead box D3*	1.7E-05	-39.1%
chr9:19923667	*Tdrd6*	*tudor domain containing 6*	2.3E-05	-48.6%
chr10:93520461 chr10:93520484	*Tanc2*	*tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2*	1.2E-03 1.4E-03	-33.1% -30.5%

Challenges

- Analysis of brain *regions* mutes effects of epigenetic alterations in specific cell types
- Translation to humans
  - confounders
  - orthologous regions
  - difficult to assess preconceptional exposures

This work is supported by the National Institute of Environmental Health Sciences of the NIH under award number P01ES022831 and by the United States EPA grant RD-83543701-0 and CR-83242401-0. The content is solely the reflection of the grantee and does not necessarily represent the official views of the NIH or the USEPA. Additional support was provided by Grant Number UL1TR001117 from the National Center for Research Resources (NCRR), a component of the NIH and NIH Roadmap for Medical Research.

American Women in Metro Atlanta Have Higher Levels of Endocrine Disrupting Plasticizers in Their Bodies Than Other African American Women

P. Barry Ryan[1], Anne L. Dunlop[2], Dana Boyd Barr[1], and Linda A. McCauley[2]

[1]Emory University Rollins School of Public Health, [2]Emory University Nell Hodgson Woodruff School of Nursing

CENTER OVERVIEW

Emory University's Center for Children's Health the Environment, the Microbiome, and Metabolomics (C-CHEM²) involves analysis of a multi-component, longitudinal birth cohort of African American women and their offspring in metropolitan Atlanta to evaluate the influence of environmental exposures on the maternal and infant microbiomes and metabolomes. We hypothesize that this may ultimately lead to neurodevelopmental sequelae in children.

RESEARCH FINDINGS

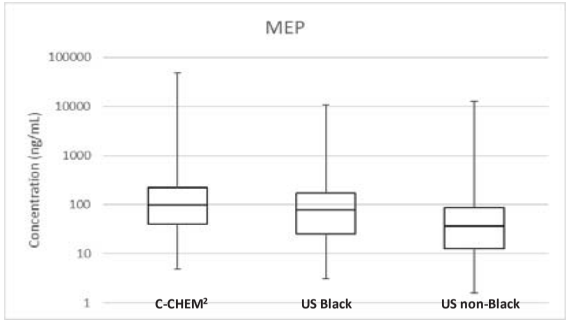
To date, 216 mothers have been enrolled in our birth cohort study and 55 children have been born. We have collected 215 urine and 210 serum samples at enrollment (8-14 weeks gestation) at the hospital; 101 urine samples, 101 dust samples and 25 air samples during the home visit at 20-24 weeks gestation; and 129 urine and 129 serum sample at the second hospital visit at 24-30 weeks gestation. Postnatal dust samples (N=61) have also been collected along with infant urine samples at 1 week (N=70), 3 months (N=49), 6 months (N=34), 12 months (N=24) of age, 18 months (N=13) between C-CHEM² and the Parent Study.

BIOLOGICAL AND ENVIRONMENTAL SAMPLES COLLECTED AND PROCESSED

Hospital Urine Visit 1	215
Hospital Urine Visit 2	129
Home Urine	101
Serum	108
Prenatal Home Dust	101
Postnatal Home Dust	61
Home Air	25
Baby Urine 1 wk	70
Baby Urine 3 mo	49
Baby Urine 6 mo	34
Baby Urine 12 mo	24
Baby Urine 18 mo	13

SUPPORTIVE RESULTS

We measured urinary BPA and phthalates in 366 urine samples to date. The geometric mean concentration of urinary mono-ethylphthalate, a metabolite of diethylphthalate that is used in many personal care products, was almost 30% higher than the national average for African American women of reproductive age and nearly 3 times the levels found in non-African American women in the US population. *Note the log scale in the figure.*



Similarly, mono-butyl phthalate was higher in our population than in African American or non-African American women in the US population. Notably, metabolites of di-2-ethylhexylphthalate were about 30% lower in our population than in the general US population.

	BPA	MEP	MBP	MiBP	MBzP	MEHP	MEOHP	MEHHP	MECPP
Number of Samples	366	288	287	278	287	267	287	286	288
Mean	2.34	422.53	24.75	16.18	15.56	4.36	6.67	8.78	10.67
Standard Deviation	7.73	47603.83	38.38	20.31	27.67	6.67	10.05	13.76	14.18
Minimum	0.2	4.97	0.43	0.08	0.09	0.07	0.06	0.38	0.28
Maximum	139.69	1443.26	374.29	136.37	222.66	58.2	112.97	169.55	114.58
LOD	0.02	0.2	0.2	0.1	0.1	0.1	0.2	0.2	2.5

OTHER FINDINGS

In addition to phthalates and alkylphenols, we have measured PBDEs, cotinine and pesticide metabolites in a subset of our population to survey exposures. PBDE 47 was detectable in 100% of the samples analysed with frequent detection of PBDEs 99 and 100. Urinary cotinine levels were higher than expected as few women report smoking during pregnancy. Despite the self-report of not smoking, about 30% of the samples tested fell within the range of smokers. Pesticides metabolite levels were higher than US population levels likely reflecting more prevalent use of pesticides in the Southeast.

CHALLENGES

Developing a messaging protocol to report study findings to participants has been challenging. Participants have been very engaged in the study and are very interested in their personal results and in the overall study results. However, developing a message that is accurate, informative and contextual has proven difficult. We are developing several templates for reporting results and plan to seek community advisory board input on the more effective format to use. Please see our COTC Presentation.

ACKNOWLEDGEMENTS

This work was supported by NIEHS: P50ES026071 and EPA: 3615301.

Obesity and Diet as Susceptibility Factors to Air Pollution Exposure

Meredith McCormack MD MHS, Greg Diette MD MHS, Jessica Rice, MD, Vsevolod Polotsky MD, Laura Paulin MD MHS, Emily Brigham, MD MHS, Michelle Eakin PhD, Cynthia Rand PhD, David Wu MD, Ashraf Fawzy, MD, Nirupama Putcha MD MHS, Kirsten Koehler, PhD, Nadia Hansel, MD MPH

INTRODUCTION

The Center for Childhood Asthma in the Urban Environment is currently investigating the role of obesity and diet as determinants of susceptibility to air pollution among children with asthma. This is a key step in achieving the Center's overall goal of developing strategies to reduce susceptibility and exposure to the harms of indoor air pollution.

Obesity Modifies the Effects on Secondhand Smoke on Pediatric Asthma Symptoms

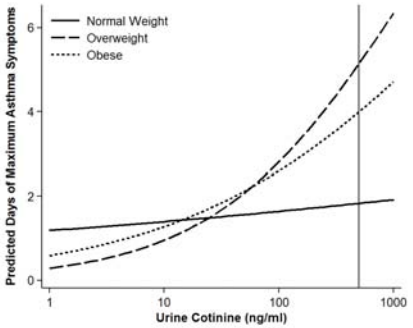
METHODS

- Two independent cohorts of 150 Mouse Allergen Asthma Cohort Study and 162 in the DISCOVER study of children with asthma
- Both cohorts included children in Baltimore city with active asthma.
- Atopic status determined by skin or RAST
- Week-long environmental at baseline, 3, 6, 9, and 12 months;
  - Airborne nicotine and PM2.5
- Spirometry, fractional exhaled nitric oxide (FeNO), height, weight measured at each assessment period. Urine at 0,6,9 months
- Associations between SHS and asthma outcomes were modeled by GEE, and effect modification by BMI category was tested.

RESULTS

- 48% of all participants were overweight/obese.
- 49% had SHS exposure based on urine cotinine (MAACS) and 73% had detectable home air nicotine (both studies)
- Overweight/obesity modified associations between SHS and asthma morbidity
  - SHS exposure in MAACS associated with greater odds of asthma-limiting activity among obese (2.69 [1.23-5.85]) and overweight (3.25 [1.17-9.03]) compared to normal weight children (1.13 [0.66-1.91])
  - SHS exposure in Discover associated with greater trouble breathing among obese (aOR 1.43 [95% CI 1.01-2.01]) compared to overweight (1.35 [0.81-2.25]) or normal weight children (0.85 [0.61-1.21]) (p-interactions<0.1).

Figure 1. The association between increasing urine cotinine concentration and predicted days of maximum asthma symptoms per two, stratified by BMI category.



Omega-3 and Omega-6 Intake Modify the Effects of Indoor PM on Pediatric Asthma Symptoms

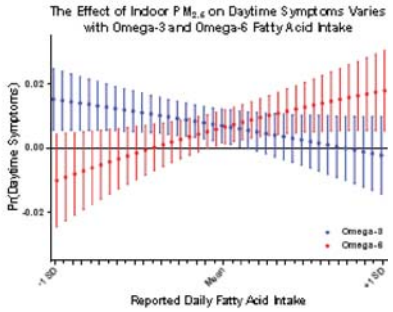
METHODS

- 137 inner-city children with asthma enrolled in the Asthma Diet Study
- Home air monitoring for one week at baseline, 3, and 6 months
- Dietary intake assessed at each monitoring period via a Baltimore-specific food frequency questionnaire (FFQ).
  - Average daily intake of omega-3 and omega-6 derived from FFQ.
- Daily symptom diary each week-long period. Presence of trouble breathing, bothered by asthma, activity limited by asthma dichotomized to present/absent.
- Associations between indoor PM and asthma outcomes were modeled by GEE, and effect modification by omega 3 and 6 intake was tested
- Models adjusted for age, gender, BMI, asthma severity, caloric intake, caregiver education level, ICS use, and season.

RESULTS

- Mean age 9.5 years (SD 2.2), 64% female, 96% African-American, majority had public insurance (91%)
- Mean omega-6 levels [5.2 g (SD 4.1 g)] and and omega-3 [0.36 g (SD 0.19)].
- Mean $PM_{2.5}$ level 34 $\mu g/m^3$ (SD 32)
- Increasing omega-3 intake associated with *reduced* effect of indoor $PM_{2.5}$ on daytime symptoms (p-interaction <0.05)
- Increasing omega-6 intake associated with *increased* effect of indoor $PM_{2.5}$ on daytime symptoms (p-interaction <0.05)

Figure 2. Conditional marginal effects of indoor $PM_{2.5}$ on daytime symptoms varies by intake level of omega-3 and omega-6 fatty acids among children with asthma.



Obesity leads to the development of Airway Hyper-responsiveness in Mice

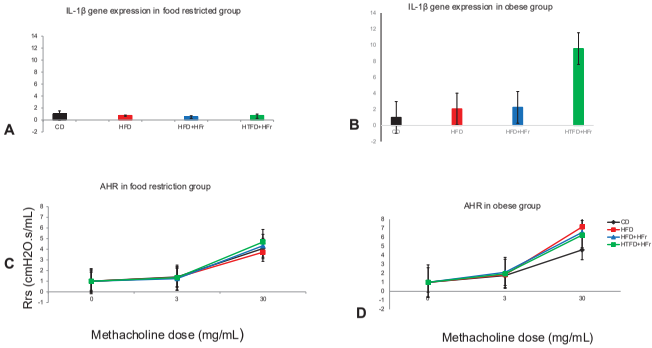
METHODS

- 64 C57BL/6J male mice (Jackson Labs), 6-8 weeks old, were studied.
- n=32 for the obese mice group, n=32 for the food restriction group
- 8 mice in each group were fed with either chow diet (CD), high fat diet (HFD), high fat diet with 30% fructose (HFD+ HFr) or high trans-fat diet with 30% fructose (HTFD+ HFr). In food restricted group, all mice were weight matched to CD mice and provided limited amount of food twice a day.
- After 8 weeks of exposure to different diets mice were anesthetized with intraperitoneal ketamine and succinylcholine. Tracheostomy was performed and mice were attached to computer controlled ventilator (Flexivent) to calculate airway hyper-responsiveness (AHR). Lung resistance (Rrs) was measured at baseline and after methacholine aerosol challenge (1,3,10,30 mg/ml).
- Mice euthanized and bronchoalveolar lavage (BAL) was performed and IL-1β were measured . Blood was then collected and lungs were harvested.

RESULTS

IL-1 β gene expression was increased in lung tissue of obese mice on hypercaloric diets, whereas no increase was seen in food restricted mice (P-value<0.05) (**Fig 3A and B**). In food restriction group there was no difference in AHR in all diets. However in obese group, there was significant increase in AHR at 30 mg of methacholine in all hypercaloric diets. The Rrs was 7.1 cmH2O.s/mL in HFD, 6.8 cmH2O.s/mL in HFD + HFr, 6.24 cmH2O.s/mL in HTFD + HFr and 4.59 cmH2O.s/mL in CD (p-value >0.05). The AHR in all diets was normalized to CD. (**Fig 3C and D**).

Figure 3: Obesity increases IL-1β gene expression and AHR regardless of the type of hypercaloric diet consumed **(Fig B and D)**. High fat diet had no effect on IL-1β gene expression or AHR if calorie restricted and not leading to obesity **(Fig A and C)**



Challenges and Implications

- Conducting home based environmental research requires building trust and ensuring two way communication. The work of our community outreach core with the input of the Community Research Advisory Council has built bridges and fostered trust that has enabled us to successfully complete these projects.
- The study of diet, obesity, and indoor pollution is complex. We have used unique study designs, including dietary feeding studies and air pollution reduction strategies in ongoing work, to perform studies that will have the ability to build an evidence base supporting causality.

Center for Research on Early Childhood Exposure and Development in Puerto Rico (CRECE)

John Meeker, José Cordero, Deb Watkins, Zaira Rosario, Carmen Vélez, Gredia Huerta-Montanez, Emily Zimmerman, Phil Brown, Helen Suh, April Gu, Akram Alshawabkeh

Presented by:

The University of Georgia · Northeastern · UPR Universidad de Puerto Rico · earthsoft · Silent Spring Institute

Center Description

CRECE is a Children's Environmental Health Center that studies how mixtures of environmental exposures and other factors affect the health and development of infants and children living in the heavily-contaminated island of Puerto Rico—an underserved, highly-exposed, and low-income population with significant health disparities. CRECE recognizes that many exposures including air quality, water quality, consumer product use, and psychosocial dynamics that can combine to create adverse health effects during infancy and childhood. CRECE is using a holistic strategy known as the "exposome" that captures the totality of the environment. As a multi-project Center, CRECE will couple air-pollution epidemiology (Project 1), high throughput toxicity screening of multi-media pollutant mixtures (Project 2), and biomarker epidemiology (Project 3) to analyze the impacts of early life exposure on fetal/child health and development, taking into account environmental, clinical, social, demographic, behavioral, dietary, and other factors. CRECE's mission is to be a vital and informative children's environmental health resource for researchers, cohort participants, the broader underserved Puerto Rican community, and beyond.

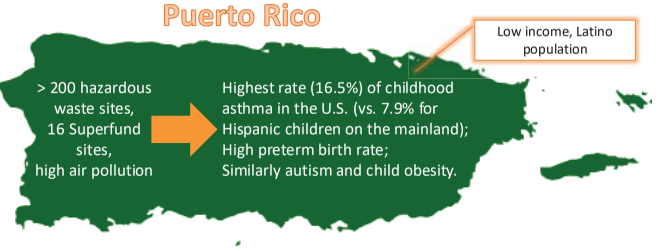
Other Preliminary Research Findings:

Follow-up of children is ongoing, we are collecting data on:

Health Measure	Study Visits								
	Prenatal (week)			Birth/ Post-Delivery	Child (age in years)				
	16-20	20-24	24-28		0	1	2	3	4
Demographic	✓	✓	✓	✓	✓	✓	✓	✓	✓
Medical Records	✓	✓	✓	✓	✓	✓	✓	✓	✓
Maternal Stress	✓	✓	✓	✓	✓	✓	✓	✓	✓
Birth Outcomes				✓					
NNS				✓					
Developmental Measures				✓	✓	✓	✓	✓	✓
Respiratory Symptoms				✓	✓	✓	✓	✓	✓

* Measurements obtained as part of CRECE indicated by black ✓ and as part of PROTECT by red ✓

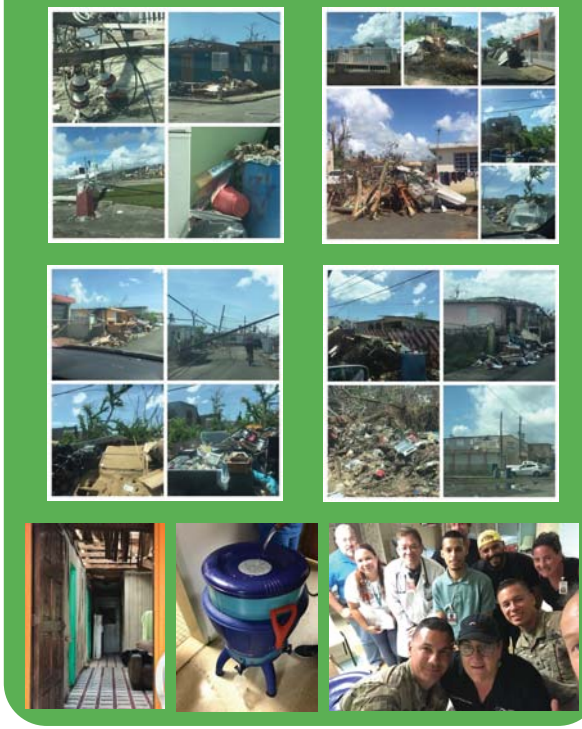
Puerto Rico



Challenge: Hurricane Maria

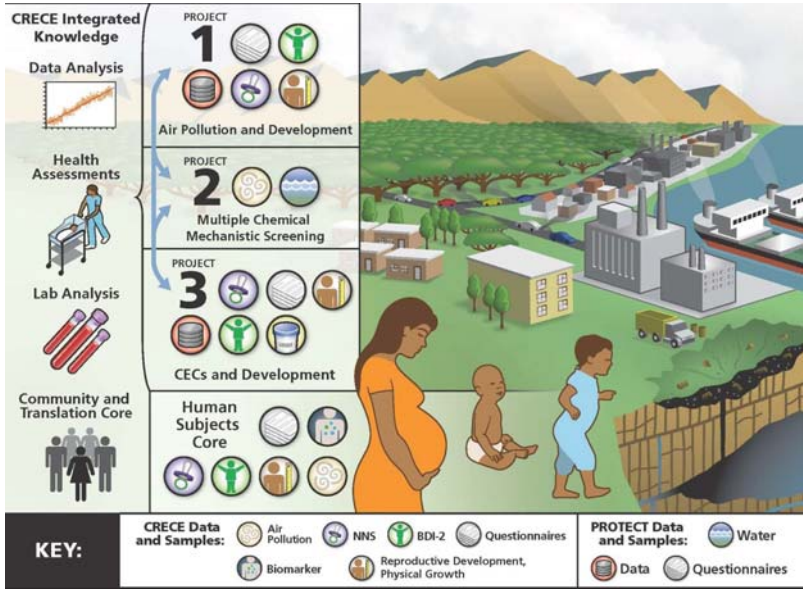
Hurricane Maria left a devastating path of destruction throughout the island that continues to be an extremely serious humanitarian and public health crisis. Lack of electricity and access to clean water and other resources remains a huge concern. CRECE researchers and staff in Puerto Rico have been on the front lines of these recovery efforts.

Photo Credits: Gredia Huerta-Montanez, Carmen Vélez, Colleen Murphy



Headline:

Exposure to Triclosan in Pregnancy is Associated with Increased Inflammation



Methods:

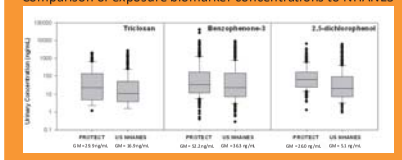
As part of the PROTECT cohort study, pregnant women were recruited early in pregnancy (<20 weeks gestation) between 2010 and 2012 in 7 prenatal clinics and hospitals in Northern Puerto Rico. At the initial study visit (Visit 1; 16-20 weeks gestation) women provided urine and blood samples and filled out detailed questionnaires. At Visit 2 (20-24 weeks) a second urine sample was collected, and at Visit 3 (24-28 weeks) both urine and blood samples were collected again. Women were followed until delivery and birth outcome data was recorded.

All urine samples were analyzed via LC-MS/MS at the National Center for Environmental Health of the CDC for five phenols: bisphenol A (BPA), triclosan (TCS), benzophenone-3 (BP-3), 2,4-dichlorophenol (2,4-DCP), and 2,5-dichlorophenol (2,5-DCP); and three parabens (butyl paraben (B-PB), methyl paraben (M-PB), propyl paraben (PPB). Specific gravity was also measured in each sample to account for urinary dilution.

For 120 subjects, plasma samples (N=215 total samples) from visits 1 (N=119) and 3 (N=96) were available for measurement of C-reactive protein (CRP) as well as 4 cytokines (IL-1β, IL-6, IL-10, and TNF-α). For 58 subjects, urine samples (N=162 total) from visits 1 (N=58), 2 (N=54), and 3 (N=50) were analyzed for 8-hydroxydeoxyguanosine (8-OHdG) and 8-isoprostane as indicators of oxidative stress. Linear mixed models were used to estimate associations between exposure and inflammation markers, adjusting for visit number, maternal pre-pregnancy BMI, education, and specific gravity.

Results

Comparison of exposure biomarker concentrations to NHANES



Product use in relation to exposure biomarker concentrations

Exposure Biomarker	Product used in previous 48 hours	Yes, ng/mL (Geo Mean)	No, ng/mL (Geo Mean)	P-value
Triclosan	Liquid Soap	36.7	18.5	0.06
	Hair Spray	50.0	27.5	0.05
BP-3	Sunscreen	503	49.8	0.001
	Hand/Body Lotion	62.7	30.1	0.05
	Mouthwash	75.5	37.2	0.03

Change in inflammation or oxidative stress marker in relation to interquartile range increase in exposure biomarker

Exposure Biomarker	IL-6		TNF-α		CRP		8-OHdG		8-Isoprostane	
	% Δ	95% CI	% Δ	95% CI	% Δ	95% CI	% Δ	95% CI	% Δ	95% CI
Triclosan	**31.5**	**8.05, 59.9**	-0.93	-10.2, 9.29	8.93	-8.50, 29.7	-2.20	-15.6, 13.3	0.52	-16.5, 21.1
BP-3	-4.81	-19.9, 13.1	-2.13	-10.3, 6.77	-16.3	-27.5, -3.42	5.28	-6.48, 18.5	**17.0**	**0.15, 36.6**
2,5-DCP	9.12	-7.76, 29.1	1.27	-6.67, 9.89	0.99	-12.6, 16.7	-7.70	-18.8, 4.93	2.49	-13.3, 21.1

The CRECE Center is jointly supported by Award Number P50ES026049 from the National Institute of Environmental Health Sciences and Assistance Agreement Number 83615501 from the U.S. Environmental Protection Agency. The content and views expressed here are the sole responsibility of the authors and do not necessarily represent the official views of the EPA, NIEHS, or the National Institutes of Health. CRECE has not been formally reviewed by the EPA, and the EPA does not endorse any products or commercial services mentioned here.

NIH National Institute of Environmental Health Sciences Superfund Research Program

"All the Research That's Fit to Publish"

The Circle Post-Observer

EARLY EDITION
Today, sunny, high 80. Tonight, clouds, low 54. Tomorrow, still really nice, welcome to the Bay.

VOL. 50 No. 18172 BERKELEY, TUESDAY, OCTOBER 24, 2017 $2.00

Toxic PCBs Still Threaten Children

Despite long-time bans, California homes remain polluted with PCBs–posing cancer risk for kids

This article was written by the Center for Integrative Research on Childhood Leukemia and the Environment.

BERKELEY, CA – During the 1970s polychlorinated biphenyls, the erstwhile industrial wonder-compounds, were banned from production in the U.S. due to concerns over possible toxicity, persistence in the environment, and bioaccumulation within the food chain. Like Frankenstein's monster, "PCBs" turned on their creators – with their engineered properties, initially so useful, ultimately becoming monstrous.

Now, forty years later, PCBs are still "*ALIVE!*" and we, the pitch-fork wielding villagers, are still reluctantly chasing the menace away from our children.

Researchers from the University of California-Berkeley sampled dust from the floors of local residences and found that PCB pollution remains widespread – with the toxins detected in each of the nearly 300 participating homes.

Subsequent research revealed that PCBs were also present in the blood of children with leukemia, in proportion to the levels observed in the house dust.

After noting that PCB levels were elevated in dust from the homes of leukemia patients, the investigators deduced the cancer-causing effect of

Continued on Page A2

A Stiff Chemical Cocktail

PCBs sold in "aroclor" mixtures, found alongside other pollutants – implicating one culprit is difficult

DURHAM, NC – R.J. Reynolds, American Tobacco Company, Liggett & Myers – all of the country's biggest cigarette makers, the purveyors of the stiffest toxic cocktails in the world – have their shops on Tobacco Road. It was here in 2015, at the birthplace of so many icky chemical concoctions, that NIEHS convened a think-tank of experts to find the best way to assess the impact of these mixtures in health studies.

Today, CIRCLE uses new approaches – weighted quantile sum regression, targeted machine learning, dimension reduction – to account for groups of

Continued on Page A3

CIRCLE investigators are taking aim on cancer. PI credit: Dr. Catherine Metayer

Aims for the 2nd cycle of CIRCLE, a Children's Environmental Health Center in Berkeley CA.

Immune Development

Find links between *in utero* exposures, fetal immune development, and childhood leukemia.

Exposomics

Discover *in utero* exposures that cause childhood leukemia using metabolomics and adductomics.

Epigenetics

Assess the impact of environmental changes to DNA methylation on childhood leukemia risk.

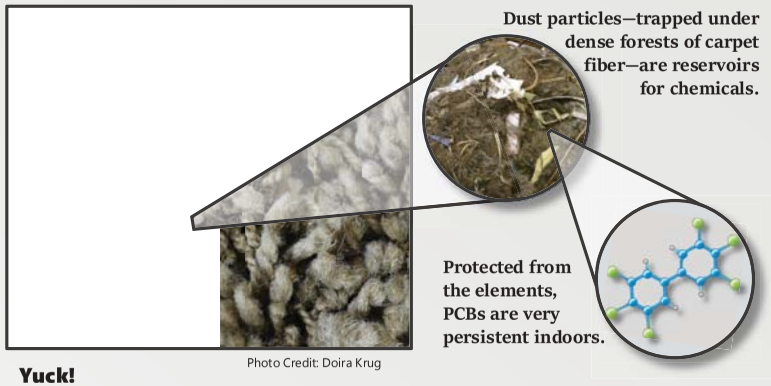


Photo Credit: Doira Krug

Yuck!

Toxic industrial chemicals are lurking deep within the carpet under your feet.

New Research To Prevent Future Cancer Cases

CIRCLE investigators evaluating abnormal immune development, epigenetic changes as causes of PCB-induced childhood leukemia

By Todd Whitehead

SAN FRANCISCO, CA – Nestled below Pacific Heights (one of the city's most affluent neighborhoods) – there is a family of mice that, by all appearances, lives in the lap of luxury. Unlimited cheese snacks, top-notch veterinary care, clean cages, and NO CATS!

The bad news? The mice have been bred to harbor a genetic weakness for cancer and the food is laced with PCBs.

They live at the Mouse Pathology Core of the UCSF Helen Diller Family Comprehensive Cancer Center and they do important work – helping to prevent future children (the human kind) from being diagnosed with leukemia.

By exposing the mice to PCBs prenatally and tracking their health, CIRCLE investigators learn more about how chemicals cause leukemia *in utero*.

Findings from the controlled rodent experiments will be corroborated by observational studies of humans, with the Center investigating two potential cancer-causing mechanisms in CA kids – abnormal fetal immune development and *in utero* epigenetic perturbations.

To help gauge the status of a child's immune development, the researchers are turning their attention to IL-10, a "cytokine" (or signaling protein) that helps immune cells communicate. They will measure this biomarker of immune health in a single blood drop collected at birth and determine the causes and consequences of stilted development.

Preliminary evidence points to a suspicious link between prenatal PCB exposures and IL-10 levels at birth.

In the same blood drop, researchers will measure DNA methylation and test whether PCBs can flip the epigenetic

Continued on Page A6

Ambient Air Pollution Impairs Immune Function which Impacts Allergy and Asthma

SK Hammond, JR Balmes, GM Shaw, K Nadeau, FW Lurmann, E Eisen, JK Mann, EM Noth, John Capitman

University of California, Berkeley; Stanford University; Fresno State; Sonoma Technology, Inc.; UCSF-Fresno

CHAPS Children's Health & Air Pollution Study

ABSTRACT

In earlier work, we showed that exposure to ambient air pollution was associated with hypermethylation of the forkhead box protein 3 (FOXP3) locus, impairing regulatory T-cell (Treg) function and increasing risk of asthma morbidity. In a later follow-up study with a larger sample size we showed that exposure to ambient polycyclic aromatic hydrocarbons (PAHs) in Fresno, CA was significantly associated with impaired Treg function, increased methylation of FOXP3, and differential expression of the FoxP3 protein, especially in children with allergies. Methylation was associated with Treg dysfunction and an increase in total plasma IgE levels. Our findings were supported by those of another group that reported FOXP3 hypermethylation was associated with diesel exhaust exposure and risk for childhood asthma. We have also shown that ambient PAH exposure is associated with increased respiratory symptoms in children with asthma as well as lower lung function in children without asthma in Fresno. In addition to exposure to PAHs, we have recently shown that short-term and long-term exposures to high levels of CO, NO_2, and $PM_{2.5}$ were associated with alterations in CpG site methylation of FOXP3 and IL-10. Collectively, these results demonstrate that increased exposure to traffic-related air pollution is associated with impaired systemic immunity and epigenetic modifications in a key locus involved in allergy: FOXP3, with a higher impact on allergic children. The results suggest that increased exposure to air pollution is linked to increased allergic and asthmatic symptoms in children.

AIMS

Project 1: To advance scientific understanding of the potential contribution of social and environmental etiologies of birth defects and preterm birth.

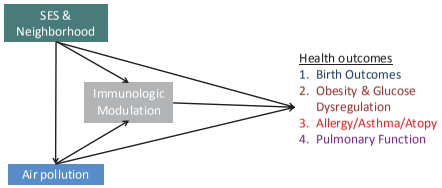
Project 2: To determine the molecular mechanisms by which immune dysregulation leads to human disease, specifically the atopic diseases of food allergy, allergic rhinitis, allergic conjunctivitis and allergic asthma in children exposed to high levels of PAHs (polycyclic aromatic hydrocarbons).

Project 3: To assess whether exposure to outdoor air pollution during childhood contributes to the development of the metabolic syndrome in adults.

Project 4: To test the hypothesis that neighborhood characteristics have a direct and quantifiable relationship with an individual's transit patterns which affect personal exposures to traffic related air pollution (PAHs, $PM_{2.5}$, and BC).

CHAPS STUDY QUESTIONS

Fig 1. The Directed Acyclic graph (DAG) shows how our four projects link together as an overarching hypothesis. Immune modulation of the part of the immune system that reflects t-regulatory cell activity is the centerpiece of all of our study questions.



RESULTS

Immunologic Modulation

Initial Hypothesis

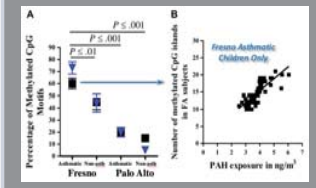


Fig 2. Nadeau et al., 2010: Exposure to ambient air pollution, specifically PAHs, is associated with hyper-methylation of the FOXP3 locus, impairing Treg cell function and increasing asthma morbidity.

CHAPS/P20

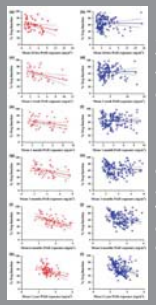


Fig 2. Hew et al., 2015: Methylation was associated with Treg dysfunction and an increase in total plasma IgE levels. Protein expression of IL-10 decreased and IFN-γ increased as the extent of PAH exposure increased.

CHAPS/P01

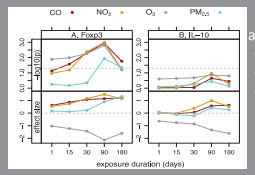


Fig 3. Prunicki et al. (submitted): Both short-term and long-term exposures to high levels of CO, O_3, NO_2, and $PM_{2.5}$ are associated with alterations in CpG site methylation of FOXP3 and IL-10.

Look at effects across 3 cohorts:
- Infants
- Children (6-8)
- Adolescents/ Young Adults

Updated PAH models
Study Obesity/ Glucose Dysregulation

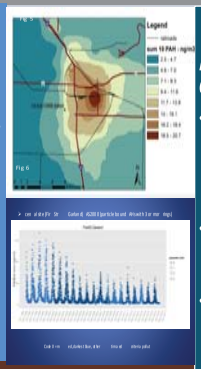
Air Pollution/Exposure Assessment

Exposure Study in Bakersfield, CA (Noth et al., 2016)

- To update our model to estimate subject specific PAH concentrations, 96-hour integrated PAH samples (n=58) were collected during four time periods at 14 locations from November 2010 to January 2011 in Bakersfield, CA.
- Individual exposures to PAHs and EC are higher near high traffic roadways and rail lines (see Figure 5)

Preliminary : Long term trends in air pollution concentrations.

- Observed a long-term declining trend in PAH concentrations in Fresno from 2000-2017. The most intense decline was from 2000-2004 (see Figure 5). Similar declines seen with NO_2 and BC.



Birth Outcomes

Neural Tube Defects in Children with Hispanic Mothers (Padula et al., 2017)

- Increased odds of neural tube defects (NTDs), particularly spina bifida, in children born in the San Joaquin Valley (1997 to 2006) whose mothers had high exposures to CO, NO, or NO_2 and lived in neighborhoods that were *more* acculturated.
- Conversely, there were increased odds of NTDs for those who had high prenatal exposure to PM_{10} and lived in neighborhoods that were *less* acculturated.
- CO, NO, and NO_2 exposures were more strongly associated with NTDs among U.S.-born vs. foreign-born Hispanic mothers.

Genetic variation in biotransformation enzymes, air pollution exposures, and risk of spina bifida **(Padula et al., submitted)**

- We evaluated the role of air pollution exposure during pregnancy and gene variants of biotransformation enzymes from bloodspots and buccal cells in a case-control study (86 spina bifida and 208 nonmalformed controls).
- Observed several gene-environment interactions between pollutants and gene variants.

Obesity/Glucose Dysregulation

Preliminary Results :
In the child cohort at baseline (ages 6 to 8, n=221):

- BMI percentile was positively associated with 6-month average NO_2, NO_x, and PAH among boys.
- 3-month average PAH and $PM_{2.5}$ associated with elevations of HbA1c (%) .
- PAH, EC, NO_2 , O3 and $PM_{2.5}$ associated with elevated 8-isoprostane levels over many averaging times .
- 3-month average NO_2 was associated with an increase in 13.7 mm Hg systolic blood pressure.

SES/Neighborhood

Lessard et al., 2016

- Neighborhood exposure to traffic pollution as well as neighborhood segregation and poverty predict risk for avoidable hospitalization and ER use among children 1-14. Children under 5 are at greatest risk for these events.

Preliminary Result:

- Neighborhood social disorganization and walkability predict asthma hospitalization and ER visits among children 1-14.
- Parents of infants and young children reported low income, food insecurity, severe crowding and inability to live on income at follow-up visits .

CHALLENGE

In 2015 we began to use mass cytomtery (CyTOF) instead of flow cytometry because of CYTOF's ability to measure more cell surface markers, increased sensitivity and cell recovery rates. However, the large volume of data obtained with CyTOF required us to obtain statistical expertise to employ analytical approaches such as clustering, dimensionality reduction, and predictive modeling.

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ACKNOWLEDGMENTS

The authors gratefully acknowledge the funders of this research, which was performed as part of the University of California, Berkeley/Stanford Children's Environmental Health Center funded by NIEHS 1P01ES022849 and EPA RD83543501 This work was also supported by the National Institute for Environmental Health Science (R21ESO14891; P20ES018173; K99ES021470) and the March of Dimes Prematurity Center at Stanford University. This publication was made possible by US EPA STAR Grants RD83459601 and RD83543501. Its contents are solely the responsibility of the grantee and do not necessarily represent the official views of the US EPA. Further, the US EPA does not endorse the purchase of any commercial products or services mentioned in the publication.

NIH National Institute of Environmental Health Sciences Your Environment. Your Health.

UC Davis Center for Children's Environmental Health

Judy Van de Water, PhD, Director

AIMS

- Leverage the vast research resources generated by the retrospective case-control study, Childhood Autism Risk from Genes and Environment (CHARGE Study) and the prospective cohort study, Markers of Autism Risk in Babies–Learning Early Signs (MARBLES Study).
- Build upon our novel findings of calcium dysregulation in cultured neurons and immune cells in the context of understanding the epigenetic effects and ramifications of toxicant exposure on gene pathways and immune function.
- Develop and apply new biomarkers of autism risk, through analysis of gestational and neonatal immune dysfunction, genetic susceptibility, and environmental exposures, to best characterize the potential health effects at various life stages and predict longer-term clinical and behavioral consequences.

CAN CYTOKINES PREDICT AUTISM?

Neonatal Cytokine Profiles Associated with Autism Spectrum Disorder Paula Krakowiak, Paula E. Goines, Daniel J. Tancredi, Paul Ashwood, Robin L. Hansen, Irva Hertz-Picciotto, Judy Van de Water

BACKGROUND: Autism spectrum disorder (ASD) is a complex neurodevelopmental condition that can be reliably diagnosed at 24 months. Immunological phenomena, including skewed cytokine production, have been observed among children with ASD. Little is known about whether immune dysregulation is present before diagnosis of ASD.

METHODS: The authors examined neonatal blood spots from 214 children with ASD (141 severe, 73 mild/moderate), 62 children with typical development, and 27 children with developmental delay as control subjects who participated in the CHARGE Study. Levels of 17 cytokines and chemokines were compared and in relation to developmental and behavioral domains.

RESULTS

RESULTS: Interleukin (IL)-1*B* and IL-4 were independently associated with ASD compared with typical development, although these relationships varied by ASD symptom intensity. Elevated IL-4 was associated with increased odds of severe ASD (OR=1.40, 95% CI, 1.03, 1.91, whereas IL-1B was associated with increased odds of mild/moderate ASD (OR=3.02, 95% CI, 1.43, 6.38). Additionally, IL-4 was associated with a higher likelihood of severe ASD versus mild/moderate ASD (OR=1.35, 95% CI, 1.04, 1.75). In many children with ASD, IL-4 was negatively associated with nonverbal cognitive ability (*B*=-3.63, SE=1.33, *p*=.04).

Table 4: Adjusted odds ratios comparing neonatal cytokine and chemokine concentrations in ASD with severe symptoms, ASD with mild to moderate symptoms, and TD in one model, N=274*

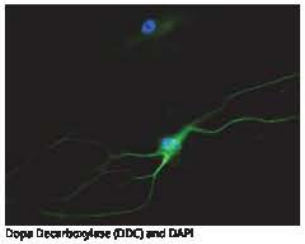
	ASD_{sev} vs. ASD_{mild}			ASD_{sev} vs. TD			ASD_{mild} vs. TD		
Cytokine or Chemokine	*OR*	*95% CI*	*P-value*	*OR*	*95% CI*	*P-value*	*OR*	*95% CI*	*P-value*
Model 1:									
IL-1B	0.59	(0.29, 1.22)	0.15	1.44	(0.88, 2.04)	0.34	**2.43**	**(0.99, 5.96)**	**0.05**
IL-4	**1.44**	**(1.08, 1.91)**	**0.01**	**1.39**	**(1.00, 1.93)**	**0.05**	0.96	(0.67, 1.39)	0.84
IL-6	0.92	(0.81, 1.04)	0.19	0.96	(0.78, 1.04)	0.17	0.99	(0.84, 1.15)	0.85
IFN-γ	0.76	(0.57, 1.01)	0.06	0.99	(0.75, 1.30)	0.92	1.30	(0.94, 1.81)	0.12
IP-10	0.69	(0.43, 1.10)	0.11	1.05	(0.64, 1.71)	0.85	1.52	(0.86, 2.68)	0.15
Model 2:									
IL-1B	**0.37**	**(0.20, 0.67)**	**0.001**	1.10	(0.59, 2.07)	0.76	**3.02**	**(1.43, 6.38)**	**0.004**
IL-4	**1.35**	**(1.04, 1.75)**	**0.02**	**1.40**	**(1.03, 1.91)**	**0.03**	1.04	(0.74, 1.46)	0.83

*Logistic regression model included selected cytokines/chemokines modeled together and was adjusted for season of birth, gestational age, years from blood spot collection to autism, and child's sex; cytokine/chemokines were ln-transformed and normalized for total protein (pg/mg total protein); values below levels of detection were imputed by multiple imputation; 276 participants comprised the following groups: 141 ASD (severe), 73 ASD (mild), and 62 TD. ASD severity was defined using ADOS comparison scores, where ≥7 indicated severe and <7 indicated mild to moderate symptoms; OR = adjusted odds ratio, CI = confidence interval

CHALLENGE & RESPONSE

Challenge: Produce human iPSC-derived neurons with mature phenotypes in a consistent and robust manner

Response: Develop alternative human cell-based modes: (1) LUHMES neuronal cell line; (2) differentiation of human epidermal neural crest cells into neurons

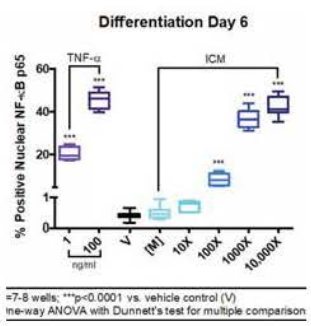


Dopa Decarboxylase (DDC) and DAPI

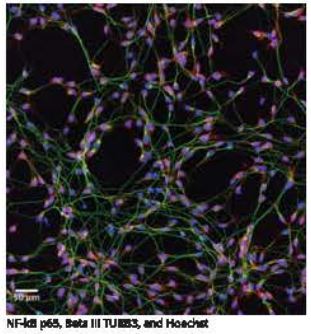
PRELIMINARY FINDINGS

Effects of Autism-Relevant Inflammatory Cytokines on Neurite Outgrowth and Toxicity in the Human LUHMES Neuronal Cell Line Lauren Matelski, Ana Cristina Grodzki, Judy Van de Water, Pamela Lein

Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) is a protein found in almost all cell types and mediates regulation of immune response by inducing the expression of inflammatory cytokines and chemokines, establishing a feedback mechanism that can produce chronic or excessive inflammation.



=7-8 wells; ***p<0.0001 vs. vehicle control (V)
ne-way ANOVA with Dunnett's test for multiple comparison



NF-kB p65, Beta III TUBB3, and Hoechst

These data suggest that inflammatory cytokines such as are seen in maternal immune activation have a direct effect on the development of neurons.

Future Studies: We will repeat the LUHMES cell work, as well as add concomitant toxicant exposure to determine if the effects are additive.

ACKNOWLEDGEMENTS

This work is funded by the US Environmental Protection Agency (Grant #83543201), the National Institute of Environmental Health Sciences (Grant #P01ES011269, Grant #R01ES015359, Grant #R21-ES021330), the UC Davis School of Medicine, School of Veterinary Medicine, and the MIND Institute. We gratefully acknowledge and thank the many families who generously donated their time to participate in the CHARGE Study.

Flame Retardants Linked to Lower Child IQ

Program on Reproductive Health and the Environment

The University of California, San Francisco (UCSF) Pregnancy Exposures to Environmental Chemicals Children's Center

October 24 – 26, 2017 NIEHS/USEPA Annual Children's Centers Meeting, San Francisco, CA

UCSF University of California San Francisco

I. Abbreviated Center Aims

- Understand how EDCS, like PBDE affect biological pathways in placenta development.
- Evaluate relationship between prenatal EDC exposures to adverse pregnancy outcomes, such as low birth weight.
- Assess how chronic psychosocial stress in pregnant women modify the chemical/pregnancy outcome associations
- Communicate the science and , harness the evolving science to healthcare, and advance prevention-based public policy.

Study Question

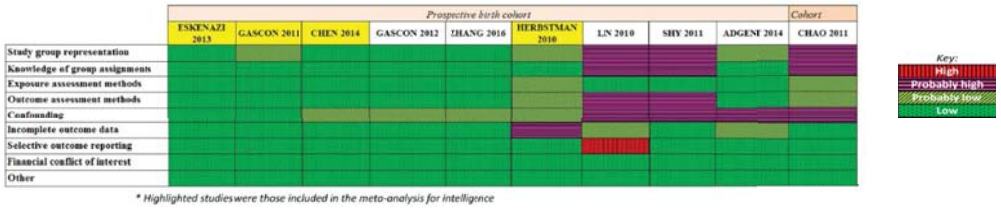
Exposure to flame retardant chemicals is associated with **cancer, reproductive, and developmental toxicity.**

Study Question: Does developmental exposure to PBDEs in humans affect quantitative measures of intelligence?

II. Research Findings

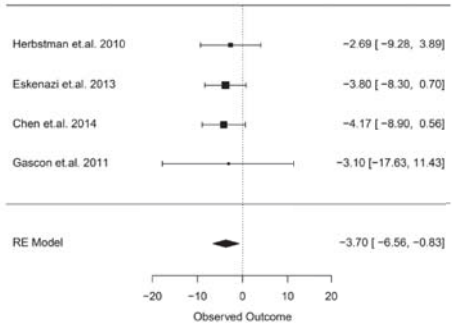
Our "BIG" result/finding from our Children's Center is from our systematic review examining PBDEs and IQ

Internal Validity (Risk of Bias) Ratings for Studies



* Highlighted studies were those included in the meta-analysis for intelligence

Meta-Analysis for PBDE exposure for IQ outcome assessed in children between 48–84 months



- Nine studies measured IQ; most were "low" or "probably low" risk of bias and the evidence was "moderate" quality.
- meta-analysis found
- **-3.7 IQ points (95% CI: -6.56, -0.83)** per 10-fold increase in PBDE exposure
- range: <LOD – 761 ng/g lipid

There is <u>sufficient evidence</u> supporting an inverse association between PBDE and IQ that warrants stronger policies to limit exposures to PBDEs to protect the public's health.

Every 10-fold increase in PBDE levels — associated with — Loss of 3.7 IQ points in children

The National Academy of Sciences (NAS, 2017) critically evaluated this systematic review and concluded there was no evidence of risk of bias and as such that it could be used as a basis for evidence integration. The NAS states, "Systematic reviews can be an important component in investigating evidence on low-dose adverse effects, and EPA can build on existing systematic reviews that are published in peer-reviewed literature."

III. Challenge

- **Challenge**: Due to inconsistent methods used to assess exposures and health outcomes across different scientific studies and the lack of reporting in published studies, we were unable to combine all included studies in a meta analysis.
- **Response**: Contacting individual study authors to obtain additional data not reported in published article. The meta analysis reported for IQ would not have been possible without the cooperation of study authors and their willingness and ability to provide additional data and information.

VI. Preliminary Research Findings from Other Center Projects

- *PBDE and its metabolites: A six year temporal trend in Northern California Pregnant Women*
  - Examining temporal trends of PBDEs and its metabolites.
  - Analyzed serum samples for seven PBDE congeners or their metabolites.
  - Found widespread exposures in participants from three time points between 2008 and 2014
  - Findings indicate that while policies to remove PBDEs from the marketplace may lead to successful declines in exposures initially, exposures could plateau and remain ubiquitous in human populations and in the environment for decades, demonstrating that use of persistent chemicals can result in exposures well past their use.

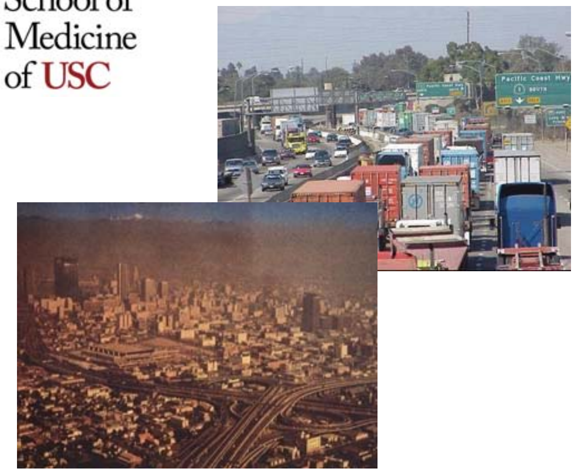
Funding for this project was provided by NIEHS P01ES022841), and the USEPA (RD83543301).

The views expressed in this article are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

Does air pollution cause childhood obesity and increase the risk of diabetes?

Rob McConnell, Frank Gilliland, Hooman Allayee, Wendy Gutschow, Jill Johnston
University of Southern California

Keck School of Medicine of USC

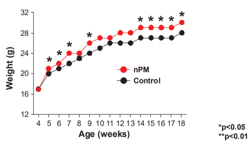


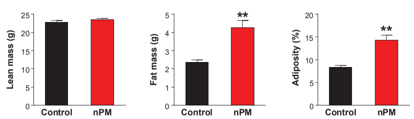
Research questions

Does *in utero* and childhood near-roadway air pollution (NRP) exposure cause:
•Childhood obesity?
•Metabolic syndrome?
•Visceral fat redistribution, ectopic fat and adipose tissue inflammation?
Are NRP effects on metabolic outcomes mediated by fat distribution and adipose tissue inflammation?

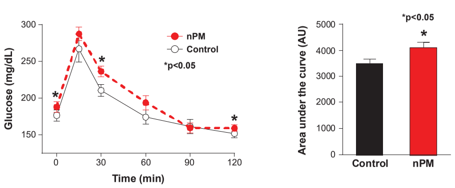
Studies in Mice

NRP (nPM) and body composition in mice

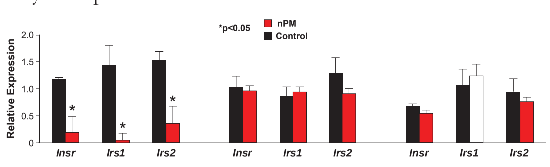




Impaired glucose tolerance

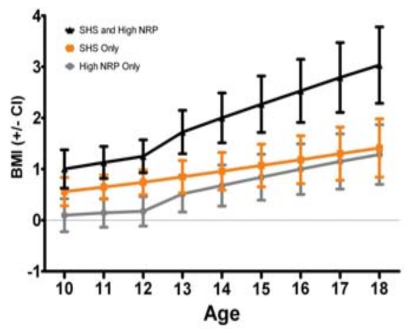


Perturbed metabolic gene expression only in adipose tissue

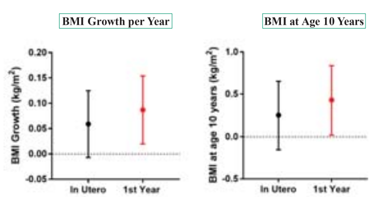


Studies in Children and Young Adults

Synergistic associations of NRP and SHS with BMI

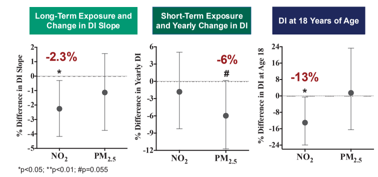


Early life NRP and BMI Age 5-10 years



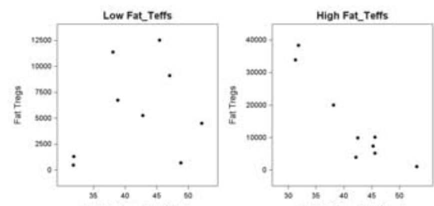
Estimates scaled to 2SD of Caline dispersion-modeled NOx (46.2 ppb), adjusted for age, sex, race, town, parental education, Spanish questionnaire, and childhood Caline exposure

NO2 and PM2.5 exposure was associated with declines in β-cell function (DI)



Estimated % difference in DI for a 1-SD difference in NO_2 (5 ppb) and $PM_{2.5}$ (4 µg/m³) with 95% CI. Adjusts for body fat %, age, sex, pubertal stage, season of testing, and social position.

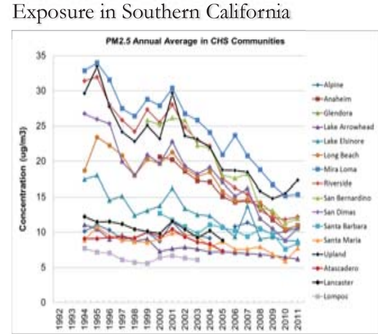
T-reg counts by lifetime average ozone exposure in high and low Teff count groups



Fasting glucose was associated with increased lifetime NRP

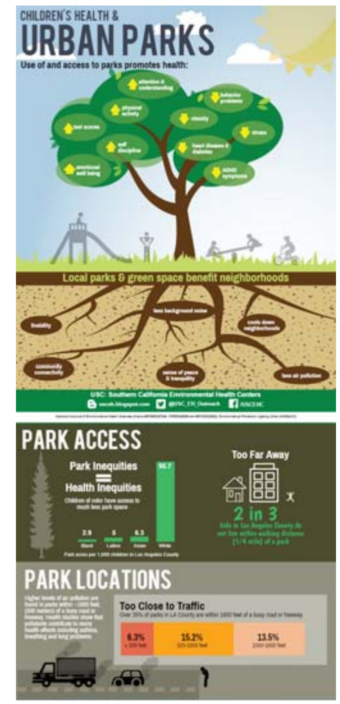
Outcome	Dispersion Modeled NOx β/2 SD NRP	SE	p-value
Clinical Fasting Glucose	0.19	0.10	0.07
Fasting Insulin*	-0.004	0.01	0.60
Insulin AUC	-0.32	0.71	0.66
HOMA-IR*	-0.002	0.01	0.85
HOMA-β*	-0.01	0.01	0.11
Matsuda	-0.001	0.07	0.99

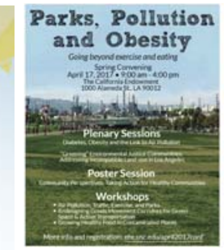
Exposure in Southern California

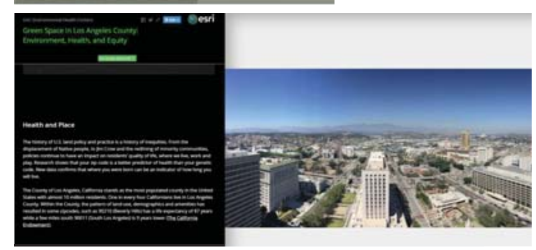


Community Outreach & Translation

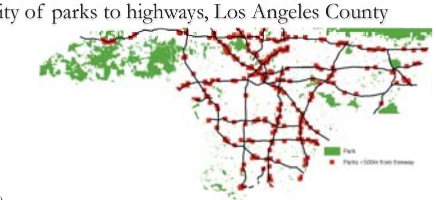
- Bridging worlds of obesity prevention, urban design and air pollution.
- Fostering dialogue between scientists and weight loss community-based organizations, parks and housing advocates, and policy makers.
- Infographics developed in partnership with community organizations to promote dialogue on risks and benefits.
- Designing an online StoryMap tool to visualize the landscape of green space, near-roadway exposure and health disparities.







Proximity of parks to highways, Los Angeles County



ehc.usc.edu

Supported by: National Institute of Environmental Health Sciences (Grant #P01ES022845), Environmental Protection Agency (Grant # 83544101)

Longitudinal exposome research reveals exposure of agricultural families to over 86 pesticides, 47 of which are identified as developmental neurotoxicants

Beti Thompson, Rachel Ceballos, Tomomi Workman, Marissa Smith, Breana Bennett, Bill Griffith and Elaine Faustman

Fred Hutchinson Cancer Research Center and University of Washington, School of Public Health, Seattle, WA

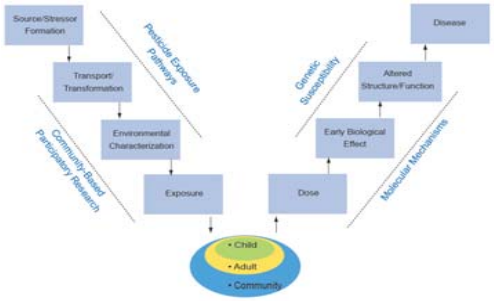
Abstract

The theme of the Center for Child Environmental Health Risks Research has been to understand the mechanisms (molecular, genetic, age, exposure, and social factors) that define children's susceptibility to pesticides, identifying the implications of this susceptibility for development and learning, and partnering with our communities to translate our findings into risk communication, risk management, and prevention strategies. This poster shows critical pathways of pesticide exposure for children in farmworker and non-farmworker families and shows how interventions are shown to reduce children's exposure to pesticides. The Center is organized using a Risk Assessment Framework that facilitates the incorporation and use of state of the art science to inform risk decisions. A critical premise for the Center is its commitment to Community Based Participatory Research and this commitment allowed us to overcome and investigate the complex patterns of exposure for short-lived and episodic pesticide use that agricultural communities can experience.

Mission and Objectives

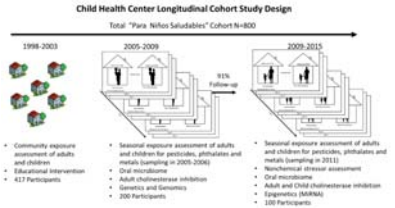
1) Improve our understanding of critical pathways of pesticide exposure for children;
2) Intervene to reduce children's exposure to pesticides;
3) Identify susceptibility factors for developmental neurotoxicity of pesticides;
4) Identify cellular, biochemical and molecular mechanisms for the developmental neurotoxicity of pesticides;
5) Provide core support for the development and application of risk assessment methods;
6) Foster partnerships and dialogue between academic researchers and the community.

Center Organization



Work in the Center is organized around the Public Health paradigm "V-diagram," which connects occurrence of disease in humans to the original source of the problem. Along the pathway from source/stressor to disease, the diagram identifies intermediate processes (which may be subject to Public Health intervention) and conditions (which may be observable for public health monitoring and hypothesis testing

Center Study Design



Our Center study design sampled farmworker and non-farmworker households over multiple days for three seasons and three different study years. Overall, the Center has worked with 800 families from the "Para Niños Saludables" Cohort since 1998.

Pesticide Measurement Using LC-MS

Pesticide Type	Pesticide Class	Pesticide
Insecticides	Organophosphate	Azinphosmethyl
		Chlorpyrifos
		Coumaphos
		Diazinon
		Dichlorvos
		Malathion
		Methamidophos
		Phosmet
		Tetrachlorvinphos
	N-Methyl Carbamate	Carbaryl
		Methomyl
		Propoxur
	Neonicotinoid	Acetamiprid
		Clothianidin
		Imidacloprid
	Pyrethroid	Cyphenothrin
		Imiprothrin
		Permethrin
		S-Bioallethrin
		Sumithrin
		Tetramethrin
	Insect Growth Regulator	Hexythiazox
		Pyriproxyfen
	Urea/Insect Growth Regulator	Novaluron
	Macrocyclic Lactone	Spinosyn A
		Spinosyn D
	Synergist	Piperonyl Butoxide
	Organosulphite	Propargite

Pesticide Type	Pesticide Class	Pesticide
Fungicides	Azole	Myclobutanil
		Propiconazole
		Tebuconazole
	Azole (Benzimidazole)	Thiophanatemethyl
	Azole (Imidazole)	Triflumizole
	Strobin	Azoxystrobin
		Trifloxystrobin
	Guanidine	Dodine
	Anilide	Boscalid
	Quinonline	Quinoxyfen
Herbicides	Urea	Diuron
	Chlorophenoxy acid or ester	2,4-D
		MCPA
		MCPP
	2,6-Dinitroaniline	Pendimethalin
	Pyridazinone	Norflurazon
		Pyridaben
Microbiocides	Chlorophenol	Triclosan
	Phenol	Na o-phenylphenate

Classification for pesticides detected in household dust. For dust analysis, 86/145 candidate pesticides were successfully measured using LC-MS. Table above shows pesticide type (e.g., insecticide, herbicide, etc.), classification (e.g., pyrethroid, azole, etc.), and name. Modified from Bennett et.

References

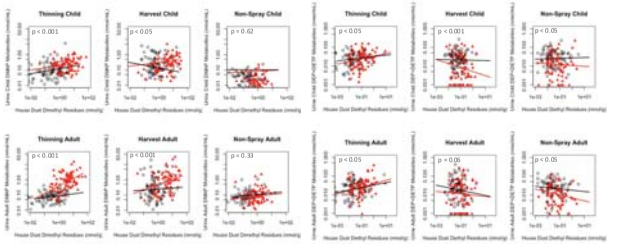
Bennett, B., Workman, T., Smith, M., Griffith, W.C., Thompson, B., Faustman, E.M. (2017). Defining the pesticide exposome: Characterizing longitudinal seasonal and occupational trends of pesticides in house dust. In progress.

Tamaro, C. M., Smith, M. N., Workman, T., Griffith, W. C., Thompson, B., & Faustman, E. M. (2017). Characterization of Organophosphate Pesticides in Urine and Home Environment Dust in an Agricultural Community. *Biomarkers*, 1-35. (Epub ahead of Print)

Smith, M. N., Wilder, C. S., Griffith, W. C., Workman, T., Thompson, B., Dills, R., ... & Faustman, E. M. (2015). Seasonal variation in cortisol biomarkers in Hispanic mothers living in an agricultural region. *Biomarkers*, *20*(5), 299-305.

Thompson, B., Carosso, E., Griffith, W., Workman, T., Hohl, S., & Faustman, E. (2017). Disseminating pesticide exposure results to farmworker and nonfarmworker families in an agricultural community: A community-based participatory research approach. *Journal of occupational and environmental medicine*, *59*(10), 982-987.

Linking Exposure with Biomarkers of Response

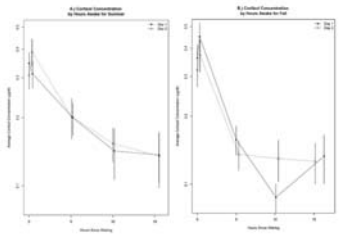


Regression of log of dimethylalkylphosphate urinary metabolites (nmol/mL) vs. log of dimethyl OP residues in house dust (nmol/g) by agricultural season. Red = Farmworker; Black = Non-Farmworker.

Regression of log of DEP+DETP urinary metabolites (nmol/mL) vs. log of diethyl OP residues in house dust (nmol/g) by agricultural season. Red = Farmworker; Black = Non-Farmworker.

Tamaro et. al. (2017)

Connecting Seasonal Work with Cortisol

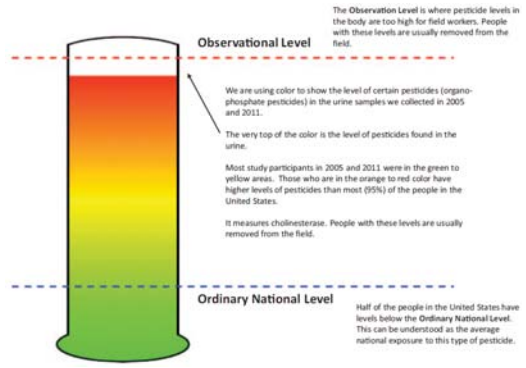


Our Center has also characterized chronic stress biomarkers in a nested cohort (n = 27) of mothers. The figures show average daily cortisol fluctuations for two consecutive days for both the summer and fall seasons for our nested cohort.

Smith et. al. (2015)

Community Outreach & Return of Results

Work in the Center is influenced by our commitment to Community Based Participatory Research (CBPR). We have disseminated research results to our study participants through the use of a thermometer graphic (below), as chosen by community members. These evaluations were conducted at a town forum. On follow-up, over 70% of participants recalled the graphic and correctly interpreted the results. This follow-up also demonstrates the effectiveness of using a CBPR approach throughout the entire research process.



Thompson et. al. (2017)

Acknowledgments: This project was supported by grant number P01-ES009601 from the National Institute of Environmental Health Sciences (NIEHS), NIH and RD-83451401 from the Environmental Protection Agency (EPA). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIEHS or EPA.

NEW!

Using storytelling to translate science for health promotion, disease prevention

A Story of Health

A Multi-media eBook

Mark Miller MD MPH, Ted Schettler MD MPH, Brian Tencza MEd, Maria Valenti, Victoria Leonard RN PhD, Marya Zlatnik MD

Download *A Story of Health* at http://wspehsu.ucsf.edu/for-clinical-professionals/training/a-story-of-health-a-multi-media-ebook/

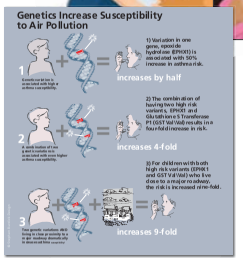
The Power of Personal Stories:

Cased-based learning has long been used in medical education. Our eBook grounds the science of health in stories of fictional people, their families, and communities to enable readers to explore the collection of risk factors for increasingly common illnesses that are a serious problem for the health of our nation.

Using the setting of a family reunion as a backdrop, we explore how multiple environments influence our health across the lifespan.

Examples:

"Brett is a nine year old boy who lives with his mother in an urban area. Like many children, Brett suffers from asthma..."



Gene-environment interactions, such as in this example from the asthma story, can have dramatic effects.

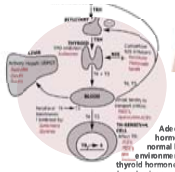
Stress-environment interactions:

"...For example, prenatal and early life exposure to social stressors, such as violence, can increase the risk of asthma as well as increase the impacts on respiratory health from allergens, air pollution, and tobacco smoke."

Stress affects our health. Watch this video by Dr. Rosalind Wright to see how social stressors, along with environmental factors, can be linked to asthma. (5 min.)

"Amelia is a 13-year-old. Like one in six young people in America, Amelia has a developmental disability..."

PRENATAL HEALTHY CARE
A Rationale for Thyroid Screening Before or During Pregnancy

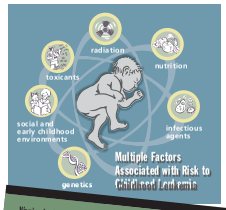


Thyroid disruption technical diagram

Adequate levels of thyroid hormone are necessary for normal brain development. Some environmental chemicals can disrupt thyroid hormone levels and function through several mechanisms.

"Stephen is a 3-year-old boy in treatment for childhood leukemia..."

Early life exposures contribute to lifelong effects



Multiple factors influence health

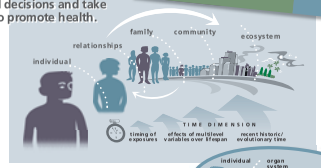
Our individual stories highlight the many ways our health is influenced by the complex environments where we live, eat, work, exercise, gather and socialize.

Although not an exhaustive account, the eBook is a presentation of current scientific evidence to help readers make informed decisions and take actions to promote health.

Individuals and families are progressively nested within communities, societies, cultures, and ecosystems. Each of these levels has significant influences on the others.

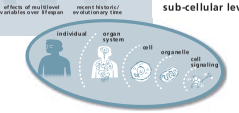
In many instances, each can influence levels of healthy or harmful biologic markers, such as inflammatory mediators or stress hormones, that can be measured in people's blood.

We call this an ECOLOGICAL FRAMEWORK because it recognizes the contribution of each level to the health status of individuals, families, communities, ecosystems.



Ecological Health Framework

The ecological health framework also extends to the sub-cellular level.



STORY IN DEVELOPMENT

Toshio and Reiko are a couple in their early 30's who have been trying unsuccessfully to have a child...

Estimated U.S. fertility statistics – 2006-2010

†Fecundity: Ability to get pregnant and carry a baby to term

OB/GYN's lack environmental health training

A survey of over 2500 OB/GYN clinicians demonstrated the need for environmental health education:

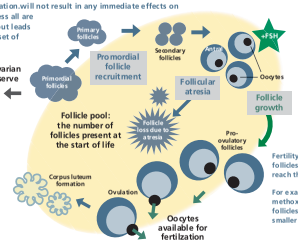
Q: Do you routinely discuss this issue as part of prenatal care?

- 78% agree they could reduce patient exposures to environmental hazards by counseling patients. But 50% say they rarely take an environmental health history
- <20% routinely ask about common environmental exposures.
- Only 1 in 15 reported any training on the topic.

Environmental exposures can affect ovarian function

Life cycle of an ovarian follicle

Destruction of primary follicles by exposures such as polycyclic aromatic hydrocarbons (PAHS, from fossil fuel combustion) and ionizing radiation will not result in any immediate effects on fertility (unless all are destroyed), but leads to earlier onset of menopause.

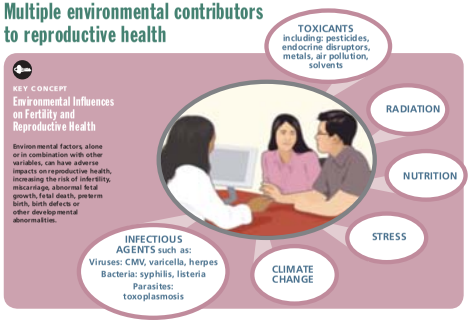


Destruction of growing follicles causes temporary infertility that can become apparent within a menstrual cycle for the large antral follicles or may take longer to become apparent if primary or secondary follicles are targeted.

Fertility resumes as earlier stage follicles mature and eventually reach the pre-ovulatory stage.

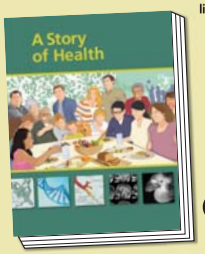
For example, the fungicide methoxychlor, targets antral follicles without affecting smaller follicles.

Multiple environmental contributors to reproductive health



About the eBook:

An interactive document with multiple chapters features prompts for embedded information and links to online resources.



Finally, a resource that clearly explains the multiple factors that influence our health across the lifespan – the natural, built, chemical, food, economic, and social environments – and how they interact with genetics and each other.

A Story of Health **is a new eBook on how to promote health and prevent disease.**

Pop-up graphics and rollover functions reveal key concepts, relevant graphics and links to videos presented by researchers – in-depth information for clinicians.

A Story of Health **is written by health experts with content relevant to a wide audience, from clinicians, to health advocates, to policy makers.**

The stories are accessible to an educated lay audience with more technical sections for scientists and medical professionals who can access free continuing education credits through the eBook.

Our goal: Improve the health of individuals, families, communities and patients.

Watch: Dr. Mark Miller discusses the Barker hypothesis (1:40 min.)

Acknowledgements: ***A Story of Health*** is a collaboration among the Agency for Toxic Substances and Disease Registry (ATSDR), the Collaborative on Health and the Environment (CHE), the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency (OEHHA), the Science and Environmental Health Network (SEHN), and the Western States Pediatric Environmental Health Specialty Unit (PEHSU) and has been supported by a range of public and private funding as well as significant in-kind contributions acknowledged in the eBook.

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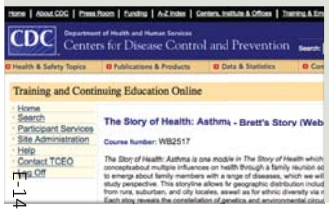
For more information contact: Maria Valenti, mvalenti@igc.org or Brian Tencza, bht1@cdc.gov.

A Story of Health Continuing Education (CE) Course via CDC Receives High Marks



CE Registrations at 10.31.16: **4,989**

Total Credit Hours: **8,919**

CE Registrant Feedback Overwhelmingly Positive

STRONGLY AGREE + AGREE = TOTAL IN %	RESPONSE: AVERAGE OF 3 STORIES
"The content and learning materials addressed a need or a gap in my knowledge or skills."	97%
"I will be able to apply the knowledge/ skills gained from this activity to develop strategies/provide interventions."	90%

COMMENTS FROM COURSE TAKERS

Anticipated changes after taking the course:

"Applying knowledge to nursing practice and in community with children/friends with asthma."

"Better able to educate patients."

"More guidance for patients in the precon-ception phase."

Feedback from a Q2/2015 CE summary

Free Continuing Education credits offered through the Centers for Disease Control and Prevention/ATSDR available for physicians, nurses, health educators and others. Visit www.atsdr.cdc.gov/emes/health_professionals/index.html.

WHAT COLLEAGUES ARE SAYING

HEALTH PROFESSIONALS RECOMMEND A STORY OF HEALTH

"Brilliant! The focus on a family and on each of their health challenges weaving in the environmental factors is masterful and I believe very effective. It is a wonderful format – and very cleverly done with a compelling story and interactive elements."

–Leslie Rubin, MD, Co director, Southeast Pediatric Environmental Health Specialty Unit, Emory University; Medical Director, Developmental Pediatrics Specialists; Research Associate Professor, Department of Pediatrics, Morehouse School of Medicine

"This is a really innovative addition to the existing textbooks on children's environmental health and could truly generate in depth learning on this complex issue. The chapter on leukemia brings together in a really cohesive way the multiple risk factors that come into play in the etiology of childhood cancer. The case based approach is particularly engaging for diverse audiences. Kudos!

–Maida P. Galvez, MD, Associate Professor Preventive Medicine, Associate Professor Pediatrics, Mount Sinai Hospital"

"It [SOH] should be required for all medical students in curriculum that ties into a life cycle approach to health... Many medical school deans and educators are looking for off the shelf materials that can be used for teaching. This is perfect."

–Robert Harrison, MD, MPH, chief of the Occupational Health Surveillance and Evaluation Program (OHSEP) in the Occupational Health Branch of the California Department of Public Health

poster design: Stephen Burdick Design